A DISSERTATION ON

"TEAR FILM ANALYSIS IN PATIENTS ON CHRONIC ANTI-PSYCHOTIC THERAPY"

Submitted to

THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY

In partial fulfillment of the requirements

For the award of degree of

M.S. (Branch III) --- OPHTHALMOLOGY

GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

APRIL 2017

CERTIFICATE

This is to certify that the study entitled **“ TEAR FILM ANALYSIS IN PATIENTS ON CHRONIC ANTI-PSYCHOTIC THERAPY ”** is the result of original work carried out by Dr.Soumya Jena, under my supervision and guidance at **STANLEY MEDICAL COLLEGE, CHENNAI.** The thesis is submitted by the candidate in partial fulfillment of the requirements for the award of M.S Degree in Ophthalmology, course from 2014 to 2017 at Stanley Medical College, Chennai.

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DECLARATION

I hereby declare that this dissertation entitled "**TEAR FILM ANALYSIS IN PATIENTS ON CHRONIC ANTI-PSYCHOTIC THERAPY**" is a bonafide and genuine research work carried out by me under the guidance of **Professor Dr. K.BASKER M.S. D.O.,** Unit chief and Head of the Department, Department of Ophthalmology, Government Stanley Medical college and Hospital, Chennai – 600001.

Date : Signature

Place: Dr. Soumya Jena

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INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Tear film abnormalities in Patients on chronic anti-psychotic therapy.

Principal Investigator : Dr. Soumya Jena,

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The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 29.09.2015 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

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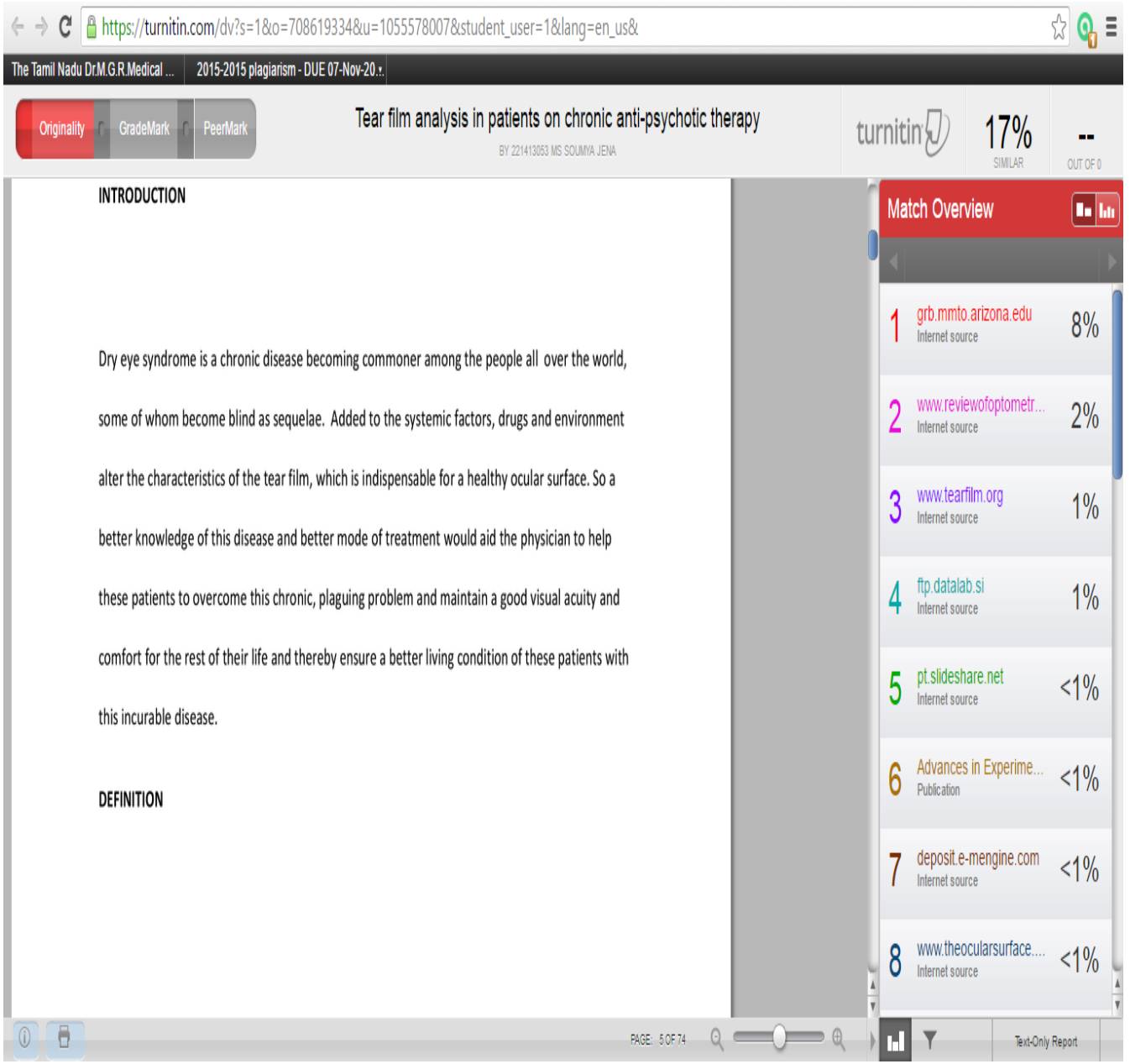
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INTRODUCTION
Dry eye syndrome is a chronic disease becoming commoner among the people all over the world, some of whom become blind as sequelae. Added to the systemic factors, drugs and environment alter the characteristics of the tear film, which is indispensable for a healthy ocular surface. So a better knowledge of this disease and better mode of treatment would aid the physician to help these patients to overcome this chronic, plaguing problem and maintain a good visual acuity and comfort for the rest of their life and thereby ensure a better living condition of these patients with this incurable disease.
DEFINITION
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PART-I

PART-II

ANNEXURES

ABBREVIATIONS

DTS	-	Dysfunctional tear syndrome
LFU	-	Lacrimal Function Unit
DSM	-	Diagnostic and statistical Manual of Mental Disorders
KCS	–	Keratoconjuctivitis Sicca
HSV	-	Herpes Simplex Virus
SJS	-	Stevens Johnsons syndrome
GVHD	-	Graft versus Host disease
OCP	-	Ocular cicatricial Pemphigoid

N/C- Nuclear/ Cytoplasmic

PART-I

INTRODUCTION

There is no doubt that in recent years, dry eye disease has become an extremely common condition that causes varying degrees of ocular discomfort and disability. Information on dry eye disease is limited due lack of uniformity in its definition and the inability of any single diagnostic test or set of diagnostic tests to confirm or rule out the condition. Thus, there has been a shift towards symptom-based assessment as the key component of clinical diagnosis.

Reported prevalence of dry eye in the literature is diverse: ranging between 7.8% in one study from western world and 93.2% in one study from Asia. This is probably because of two factors: first, the geographical location of the study population and secondly, there is no standardization of the selected population, dry eye questionnaires, objective tests and dry eye diagnostic criteria.

According to studies conducted in Northern and Eastern India, the prevalence of dry eye was found to be between 18.4 and 40.8%. One small study from Leh showed a higher prevalence of dry eye of 54% in high altitude.

Dry eye syndrome is a chronic disease becoming commoner among the people all over the world, some of whom become blind as sequelae. Added to the systemic factors, drugs and environment alter the characteristics of the tear film, which is indispensable for a healthy ocular surface.

So a better knowledge of this disease and better mode of treatment would aid the physician to help these patients to overcome this chronic, plaguing problem and maintain a good visual acuity and comfort for the rest of their life and thereby ensure a better living condition of these patients with this incurable disease.

Anti-psychotic agents are very commonly used medications in a Psychiatry setup for patients suffering from Psychoses and Delusional disorder. As these patients are on medications all through their life , side effects are seen very commonly in them. Liver is the organ most commonly affected by Anti-psychotic medications, followed by eyes. Ocular side effects include blurring of vision, dry eye, corneal deposition of drugs, stellate capsular deposits, oculo-gyric crisis etc. Of these many ocular side effects, Dry eye disease, often does not get proper attention and thus, leads to great discomfort to the patients.

NEED FOR STUDY

DRY EYE IN PATIENTS ON ANTI-PSYCHOTIC THERAPY

Antipsychotics have a significant dose related anticholinergic side effect leading to symptoms like dry mouth, blurring of vision, urinary hesitancy. Another significant side effect is dry eye which is often neglected leading to great discomfort to the patient.

Possible mechanism suggested is – Due to the anti-cholinergic action of these drugs, they block the muscarinic receptors present over lacrimal gland . This decreases the tear secretion leading to an unstable tear aqueous layer. And that is the reason for aqueous deficiency and dryness of eyes.

According to a study by Mcintosh et al, the schizophrenic patients on neuroleptics showed decreased blink rate which may be another cause of dry eye in these patients.[6]

Our study aims at dealing with this particular side effect of the Anti-psychotic agents.

HISTORICAL REVIEW

YEAR	DEVELOPMENT
5^{TH}-4^{TH} BC	Ophthalmic conditions were classified as dry or humid by Hippocrates
1888	The term xerostomia was introduced by Hadden
1892	Mikulicz syndrome was described by Mikulicz
1930	The term keratoconjunctivitis Sicca was first used by Henrique Sjogren
1936	Keratoconjunctivitis Sicca was named as Sjogrens syndrome by Duke Elder
1946	Three –layered tear film structure concept was presented by Wolff
1995	The National eye institute /industry(NEI/Industry)Dry Eye Workshop classifications
1998	Michael Stern proposed that cytokine/receptor-mediated inflammation is common to all ocular surface disorders including Dry eye
2005	Triple classification by Juan Murube
2006	Delphi approach to treatment recommendation
2007	International Dry Eye Workshop(DEWS)report

ANATOMY OF TEAR FILM

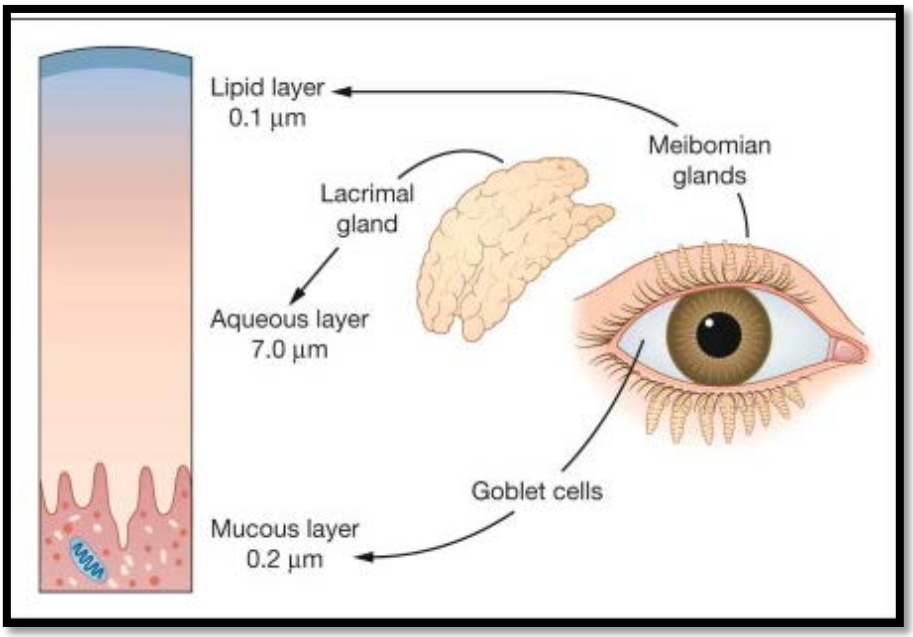
The term PRE-CORNEAL TEAR FILM was given by Wolff. It has got 3 layers:

1) LIPID LAYER: It is the outermost superficial oily layer. It is derived from secretions of meibomian, zeiss and moll glands. It forms the marginal tear strips. Lipids of low polarity like wax, cholesterol are fluid at body temperature. The high polarity lipids are negligible and constitutes of triglycerides, free fatty acids and phospholipids. Thickness of this layer is 0.1um, which increases when lids are partially closed. It prevents the overflow of tears and retards the evaporation.

2) AQUEOUS LAYER: It is the middle layer. It is secreted by the main lacrimal gland and accessory glands of krausse and wolffring. Its thickness is 10um.It forms an aqueous solution of low viscosity containing ions of organic salts, urea, glucose, biolpolymers such as enzymes, proteins and glycoproteins with proteins like lysozyme, lactoferrin, tear specific prealbumin, secretory immunoglobulin A. It has a buffering action due to bicarbonate and proteins present in it. It is rich in surface active substances like mucus glycoproteins which helps in reducing surface tension. It provides atmospheric oxygen to epithelium, washes away debris and notoriuous irritants, contains anti bacterial substances like lysozyme and betalysin.

3) MUCIN LAYER: It is the deepest layer which is produced by conjuctival goblet cells, crypts of henle and glands of manz. Also, by main lacrimal gland. It is responsible for the stability of the tear film with a thickness of 30 um (thickest according to the latest studies using confocal microscopy). The clear corneal surface is hydrophobic. Mucin gets absorbed on the surface of the epithelial cells and anchored by their microvilli forming hydrophobic surface on which aqueous and lipid layers spreads spontaneously .It lubricates ocular and palpebral surfaces leading to minimal friction during blinking and eye movements. It provides slippery surface over foreign body, and helps prevent abrasion formation.

ANATOMY OF TEAR FILM



FUNCTIONS OF TEAR FILM

* Forms a perfectly smooth optical surface on the cornea by filling in and smoothening out small surface irregularities in the corneal epithelium.

* Keeps the surface of conjuctiva and cornea moist.

* Acts as lubricant for pre-ocular surface and lids, decreasing frictional forces generated by blinking and eye movement.

* Transfers oxygen from air to cornea.

* Prevents infection due to the presence of antibacterial substances as lysozyme, betalysin, lactoferrin, immunoglobulins and other proteins in it.

* Washes away debris and noxious irritants.

* Gives a pathway to WBCs in case of injury.

DRY EYE DISEASE

DEFINITION

NEI definition (1995): Dry eye disease (DED) is a disorder of the tear film due to reduced tear production or excessive tear evaporation, which causes damage to the inter-palpebral ocular surface and is associated with symptoms of ocular discomfort and/ or visual symptoms.

DEWS Definition (2007): Dry eye disease is a multifactorial disease of the tear film and ocular surface that results in symptoms of discomfort, visual disturbance, and tears film instability with potential damage to the ocular surface. It is accompanied by increased osmolality of tear film and inflammation of the ocular surface.

SIGNIFICANCE OF THE NEW DEFINITION: The role of hyperosmolarity of tear film, inflammation of the ocular surface and effect on visual acuity found a place in the new definition which were not considered in previous definition.

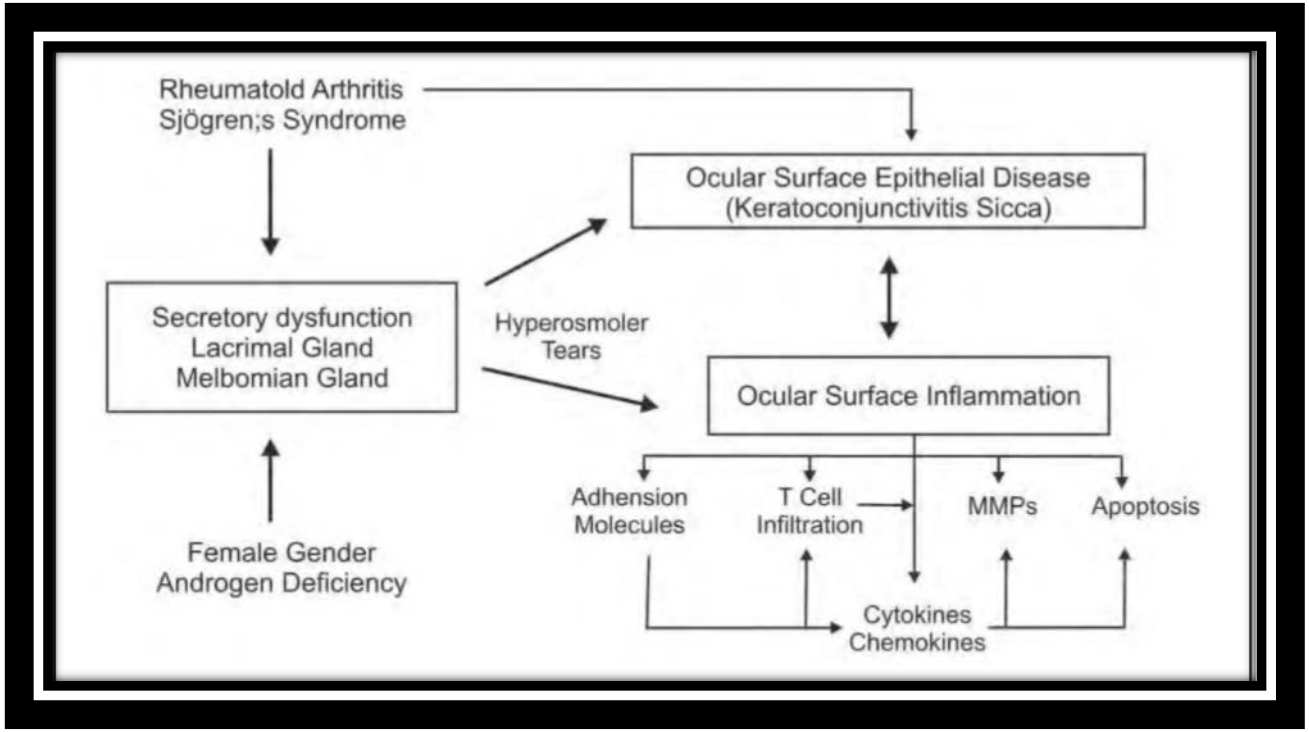
PATHOGENESIS

The lacrimal glands, ocular surface, lids, and the sensory and motor nerves that connect them, they all act as an integrated functional unit known as Lacrimal functional unit or LFU which maintains the tear production and helps to clear used tears.

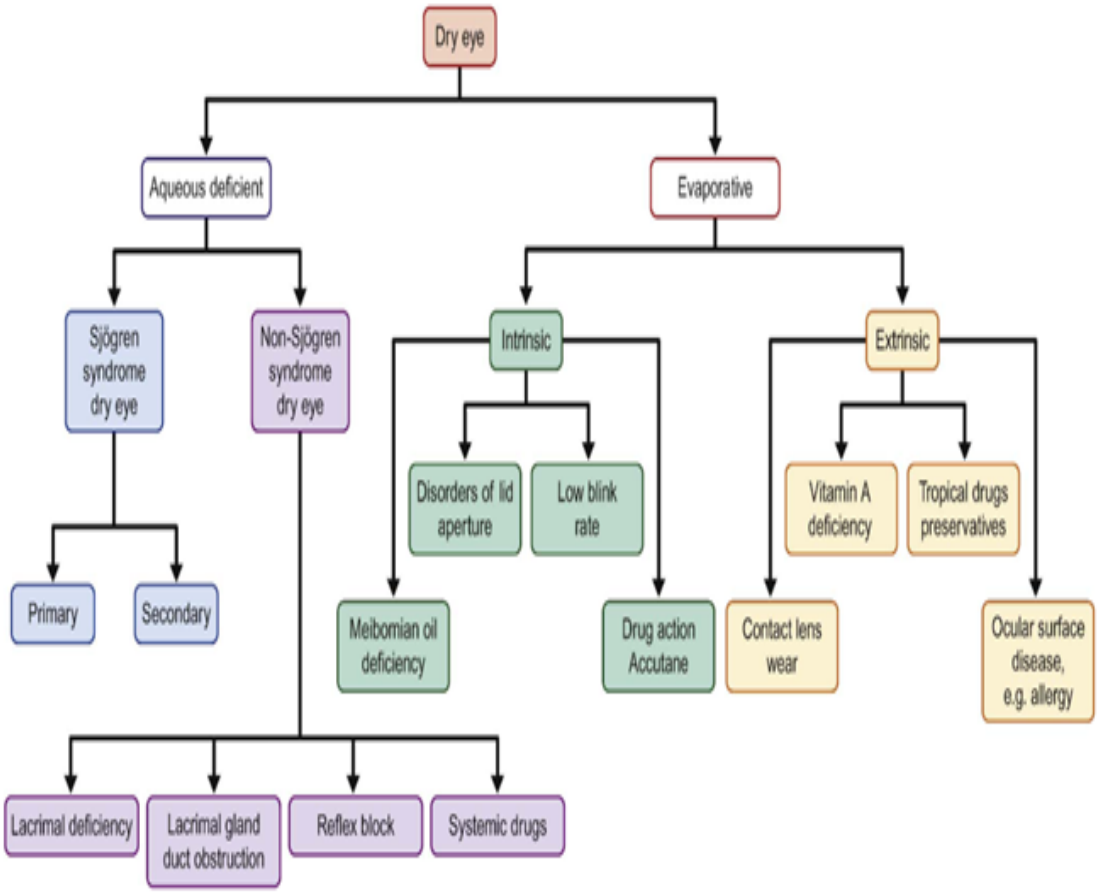
Any disease or dysfunction of this unit results in an unstable and poorly maintained tear film that leads to ocular irritation and ocular surface disease known as keratoconjunctivitis sicca (KCS).

The dysfunction of this LFU may develop from natural aging, a decrease in supportive factors (as androgen hormones), systemic inflammatory diseases (like rheumatoid arthritis), ocular surface diseases (as HSV keratitis) or surgeries which disrupt the afferent sensory nerves (as in LASIK), and systemic diseases or medications that disrupt the efferent nerves that stimulate tear secretion.

A decrease in tear secretion and clearance initiates an inflammatory response on the ocular surface that involves soluble and cellular pro-inflammatory mediators (cytokines). Research shows that T-cell lymphocytes also play a major role in the pathogenesis of KCS.


Rheumatold Arthritis
Sjögren;s Syndrome
Ocular Surface Epithelial Disease
(Keratoconjunctivitis Sicca)
Secretory dysfunction
Lacrimal Gland
Melbomian Gland
Hyperosmoler
Tears
Ocular Surface Inflammation
Adhension
Molecules
T Cell
Infiltration
MMPs
Apoptosis
Female Gender
Androgen Deficiency
Cytokines
Chemokines

CLASSIFICATION



CLINICAL FEATURES

SYMPTOMS

- Feeling of dryness, grittiness and burning that worsens during day are the most common symptoms
- Stringy discharge, transient blurring of vision, redness, paradoxical watering, photophobia may be there.
- The symptoms are usually exacerbated in conditions associated with increased tear evaporation (air-conditioning, wind and central heating) or prolonged reading which leads to reduced blink rate.

Ocular history:

• Topical medications used and their frequency like anti-histaminic, glaucoma medications, corticosteroids

• Contact lens use- type and wearing schedule

• Chronic allergic disease of the eye

• Ocular surgical history as prior keratoplasty, cataract surgery, refractive surgery ,prior lid surgeries

- Ocular surface disorder i.e. HSV infection, varicella zoster virus, OCP, SJS, aniridia, GVHD

Medical history:

• Menopause

• Systemic inflammatory diseases i.e. Sjögren syndrome, rheumatoid arthritis, systemic lupus erythematosus

• Atopy: e.g., dermatitis, rhinitis, bronchial asthma

• Systemic medications i.e. antihistamines, diuretics, hormones and hormonal antagonists, antidepressants, cardiac antiarrhythmic drugs, isotretinoin, diphenoxylate/atropine, beta-adrenergic antagonists, chemotherapy agents, any other drug with anticholinergic effects

• Other systemic conditions like sarcoidosis, lymphoma

• Chemical injury: e.g., lime burn

• Chronic viral infections: e.g., hepatitis C, HIV

• Radiation to orbit or nearby area

• Neurological conditions: Parkinson disease, Bell’s palsy, trigeminal neuralgia

• Smoking or exposure to passive smoking

SIGNS:

- **Lids-**may show Posterior blepharitis and meibomian gland dysfunction.
- **Conjunctiva** -mild keratinisation, Non specific conjunctivitis, conjuctivochalasis
- **Tear film** -In a normal eye, when the tear film breaks down, the mucin layer gets mixed with lipid but is eventually washed away. In a dry eye however, the lipid-contaminated mucin accumulates in the tear film as particles and debris that move with each blink.

The inferior tear film meniscus height is a crude measure of the volume of aqueous in the tear film. In a normal eye the meniscus height is about 1 mm, while in dry eye it becomes thin or absent.

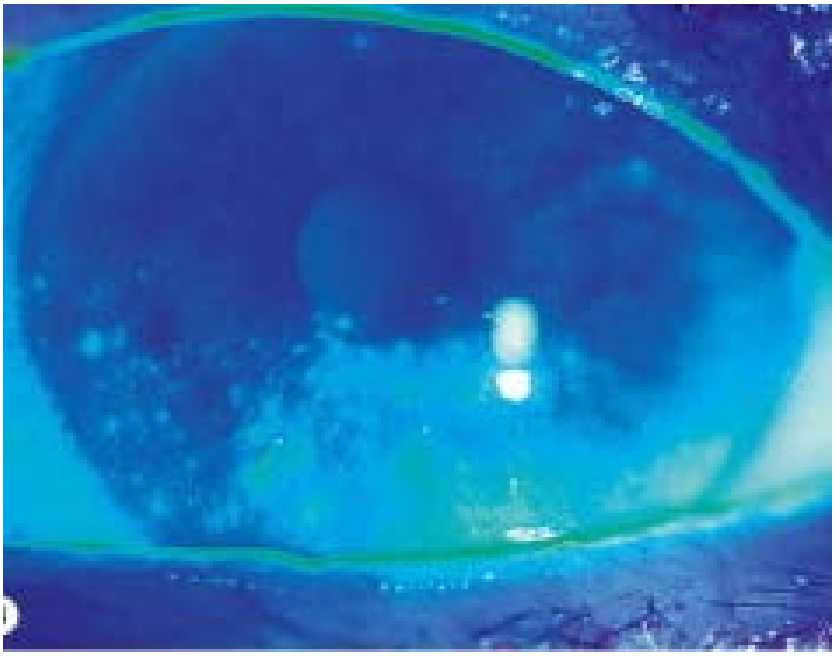
Froth in the tear film or lid margin occurs in meibomian gland dysfunction.

- **Cornea** -Punctate epithelial erosions that stain with fluorescein.

Filaments consisting of mucus strands lined with epithelium attached at one end to the corneal surface may be present which stain well with Rose Bengal. Mucous plaques are composed of mucus, epithelial cells and proteinaceous and lipoidal material and are usually seen in association with corneal filaments.

THIN TEAR FILM MENISCUS HEIGHT WITH CORNEAL STAINING

WITH FLUORESCEIN



MEIBOMIAN GLAND DYSFUNCTION

CLINICAL TESTS

1) TEAR SECRETION ASSESSMENT:

a) Schirmer's test

It is measured with special filter paper (no.41 Whatman, 5mm wide,35mm long).The paper is folded 5mm from one end & inserted at junction of middle & outer 1/3rd of lower lid and kept for 5 minutes with eyes open.

Schirmer’s Test 1:

It measures the Total (Reflex + Basal) tear secretion. Basal secretion alone is measured after anesthetizing conjunctiva. Normal value is >10 mm.

Dry Eye

Mild 10 to 6 mm

Moderate 5 to 3 mm

Severe 0-2 mm

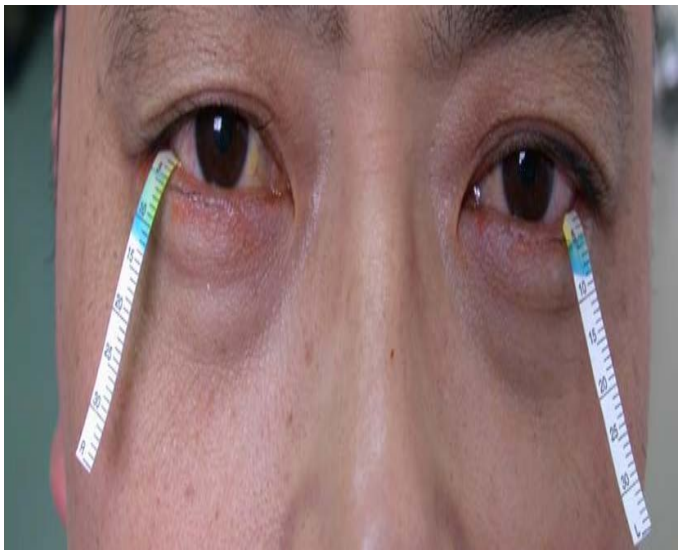
Schirmer's Test 2 :

It is done to ascertain the reflex secretion. After the strips are installed, un-anaesthetized nasal mucosa is irritated. It is then measured after 2 minutes. Less than 6mm is considered as failure of reflex secretion.

b) Phenol red test

A thread impregnated with a pH-sensitive dye is used. One end of the thread is placed in the lower lid fornix & is left to wet. It is then measured after 15 secs. The dye changes from yellow to red in colour when it comes in contact with tears. Value of < 6mm is abnormal. This test is comparable to schirmer's test and takes less time to perform.

SCHIRMER’S TEST



PHENOL RED TEST

1) TEAR VOLUME ASSESSMENT

Tear meniscus height:

Marginal tear strip is continuous, concave meniscus between eyelid margin & inferior bulbar conjuctiva, where lid touches the globe and can be easily visualized in Slit Lamp Examination. A tear film height of 0.5 to 1mm is considered normal. Scanty, discontinuous, absent tear meniscus is an important sign of dry eye & tear deficiency.

TEAR MENISCOMETRY: Tear meniscus is seen noninvasively using a tear interference device . Tear interference image is then captured with a digital video camera. The quantification of the height & volume of lower lid meniscus is done.

3) TEAR CLEARANCE ASSESSMENT

Fluorescein clearance test (FCT)

A normal tear turn over rate is important for removing inflammatory cytokines and providing fresh growth factors. Delay in tear clearance strongly correlates with ocular irritation symptoms independent of aqueous tear production. It is done by putting 5 µl of fluorescein on the ocular surface and measuring the residual dye with a Schirmer strip placed over the lower lateral lid margin at intervals of 1, 10, 20 and 30 minutes. The presence of fluorescein on each strip is

examined under blue light and compared to a standard scale or measured using fluorophotometry. In normal eyes the value will have fallen to zero after 20 minutes

4) TEAR FILM STABILITY

TEAR FILM BREAK UP TIME- It is done by moistening a fluorescein strip with saline & applying it to lower fornix. After several blinks, tear film is examined using cobalt blue filter in slit lamp. The interval between last blink & appearance of first randomly distributed area of dark discontinuity is measured.

TBUT<10 secs is abnormal. It is seen in both aqueous deficiency & meibomian gland disease.

NON INVASIVE TBUT: Done with the help of keratometer, keratoscope, tearscope. Measurement takes longer time than fluorescein TBUT. <15 secs is considered dry eye.

5) OCULAR SURFACE DAMAGE ASSESSMENT

a) Tear film osmolarity: Values higher than 312 mOsol /litre are diagnostic of dry eye.It is 90% sensitive, 95% specific. A commercial osmometer specifically designed to test nanometer volume of tear is now in use but is not widespread due to cost factor.

CONDITION	EXPECTED RANGE OF VALUE
Normal	<312 mos/l
Borderline dry eye	312-323 mosm/l
Moderate/Severe dry eye	>323 mosm/l

b) Ocular surface dye staining

It is done to detect ocular surface epithelial pathology associated with dry eye:

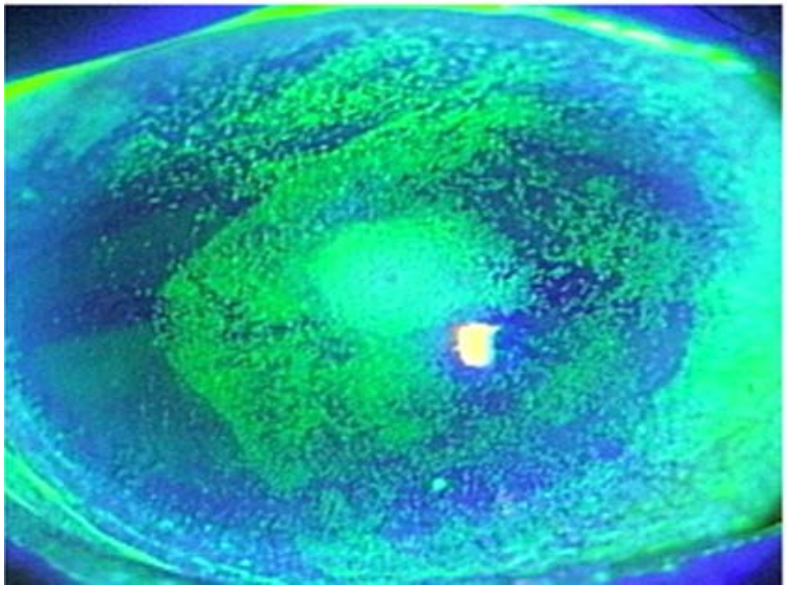
- Fluorescein sodium
- Rose bengal
- Lissamine green

FLUORESCEIN DYE TEST- most commonly done. It stains the cornea more than conjunctiva, in the interpalpebral area.it leads to significantly greater amount of staining in Sjogren's disease and aqueous tear deficiency .

ROSE BENGAL STAINING: It stains tissue by penetrating into intercellular spaces. It stains the devitalized epithelial cells and the healthy epithelial cells when they are not protected by a layer of mucin. Conjunctiva stains more intensely than the cornea.In interpretation of rose bengal staining in dry eye is based on two factors(Van Bijsterveld score)-intensity and location. Its graded on a scale of 0 – 3 in 3 areas

LISSAMINE GREEN-Its staining pattern is identical to Rose Bengal, but produces much less irritation

FLUORESCEIN STAINING



ROSE BENGAL STAINING

c) Conjuctival impression cytology:

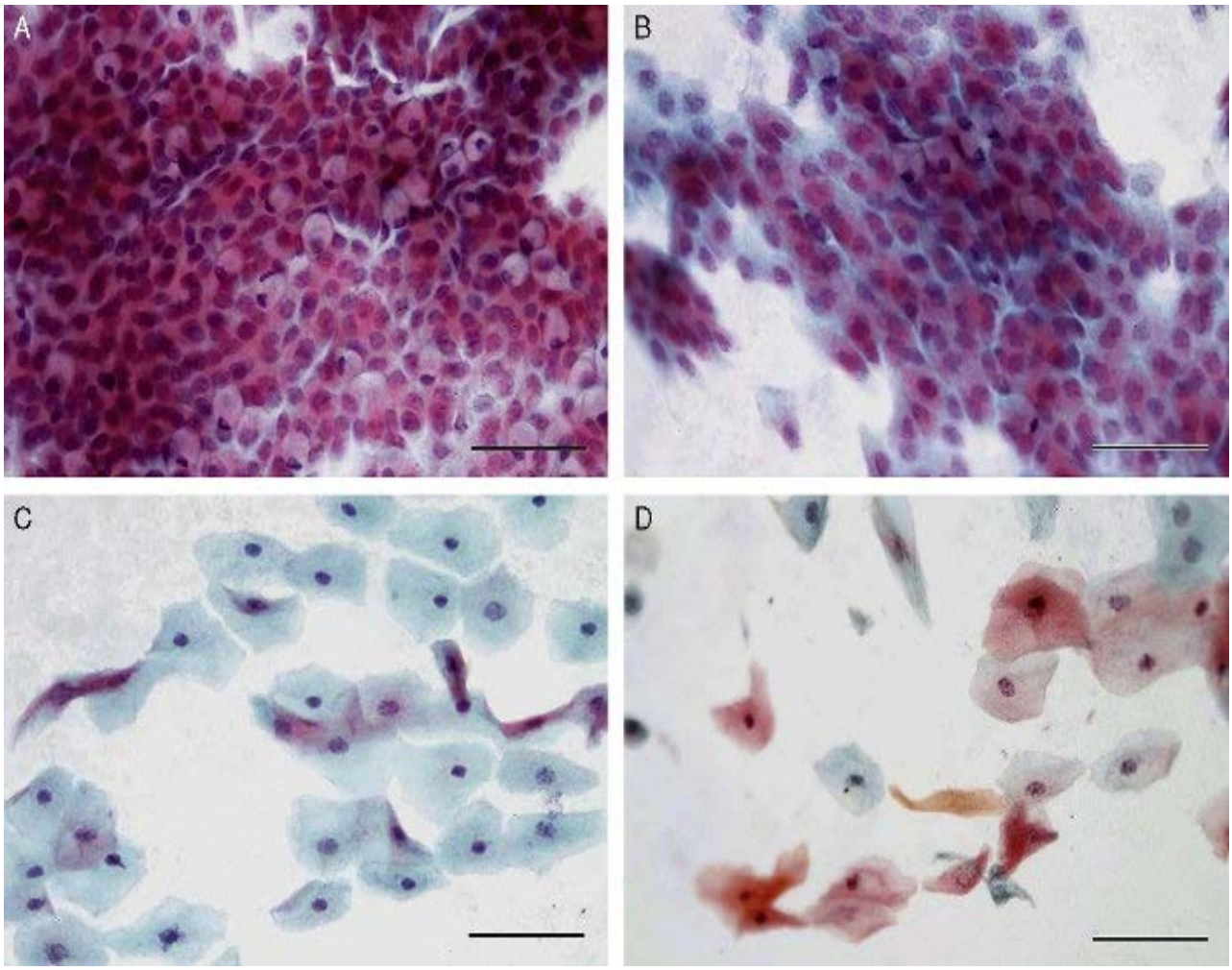
Its a non invasive technique.A drop of proparcaine is instilled and conjuctival impressions are taken by applying cellulose acetate filter paper to remove superficial layers of epithelium which is then air dried & stained with PAS & haematoxylin /papanicalou stain and examined under electron microscope.

Findings of cytology graded are from 0-3

- Grade 0-Normal number of goblet cells and normal appearing epithelial cell with N/C ratio of 1:2
- Grade 1-350-500 goblet cells and more polygonal epithelial cells with normal N/C ratio of 1:3
- Grade 2-100-350 goblet cells and abnormal epithelial cells with N/C ratio of 1:4
- Grade 3-No goblet cells and keratinized epithelial cells with N/C ratio of 1:6

Grade higher than 1 are abnormal.

CONJUCTIVAL IMPRESSION CYTOLOGY



d) Conjunctival and corneal sensation :

Decreased corneal sensation can be both the cause and the effect of dry eye. Sensory denervation may lead to dry eye by reducing the afferent signal, reducing the blink rate, altering growth and differentiation of ocular surface through trophic influence of trigeminal nerve, Auto immune sensory neuropathy and sensory neural degeneration due to inflammation or chronic over stimulation. CORNEAL ESTHETIOMETRY can be done for the same.

e) Tear protein analysis

In small unstimulated tears protein levels are 2gm% and in stimulated tear- 0.3-0.7gm%. Various proteins that are found in normal tear are IgG, Albumin, transferrin, alpha 1 antitrypsin, beta 2 microglobulins , lysoyme, lactoferrin, IgA.

f) **Crystallization /Ferning test:**

Tear film composition affects the way in which a collected sample of tear dries on a glass slide. This test is based on mucus ferning patterns. Tears are collected in a glass capillary & placed on a glass slide & left to dry at room temperature. The sample is then observed in white light or by polarized microscopy & classified in to various grades depending on crystallization. The tears of dry eye patient exibit less ferning than those of normal patients. Test may reflect the quality of tear protein profile.

Table 4. Characteristic Findings for Dry Eye Syndrome Diagnostic Testing[33]

	Test	Characteristic Findings
Aqueous Tear Deficiency	Tear break-up time	Less than 10 seconds considered abnormal
	Ocular surface dye staining	Pattern of exposure zone (interpalpebral) corneal and bulbar conjunctival staining typical
	Aqueous tear production and clearance (Schirmer test)	5 mm or less for Schirmer test with anesthesia considered abnormal
	Fluorescein clearance test/tear function index	Test result is compared with a standard color scale
	Lacrimal gland function	Decreased tear lactoferrin concentrations
	Tear osmolarity	Increased
Evaporative Tear Deficiency	Tear break-up time	Less than 10 seconds considered abnormal
	Ocular surface dye staining	Staining of inferior cornea and bulbar conjunctiva typical
	Tear osmolarity	Increased

TREATMENT

The aims for treating dry eye disease include:

- To diagnose the dry eye condition and recognise its various causes.
- To educate and involve the patient in the management of these chronic disease states.
- To establish an appropriate therapeutic regimen.
- To prevent long term complications such as infections or permanent structural damage

This can be achieved by–

1) Tear supplementation
2) Tear conservation
3) Tear stimulation

I) TEAR SUPPLEMENTATION

1) Artificial Tear substitutes:

An ideal artificial tear would have the same metabolic, optical and physical characteristics as that of natural tears.[5]Additionally, it would have a long ocular residence time and would contain therapeutic additives to treat primary and secondary damage to the eye.[5]

3)Lacrimal occlusive devices:

a) Temporary:

Inserting collagen plug into canaliculi which dissolve over weeks. Main aim is to ensure epiphora does not occur following permanent occlusion. At first, inferior puncta alone is occluded and patient is asked to review after 1 to 2 weeks. If patient is asymptomatic, without any epiphora, plug is removed & inferior canaliculi is permanently occluded. In cases with severe KCS, both inferior and superior canaliculi needs to be plugged.

b) Reversible:

Prolonged occlusion with silicone or long lasting (2-6 months)plug. Its disadvantage being extrusion, granuloma formation,distal migration,infection.

c) Permanent occlusion:

Its done in patients with Severe dry eye(who had positive response with temporary occlusion without epiphora). It is avoided in young patients who have reversible pathology. All 4 puncta are occluded at same time. Done following punctal dilatation by coagulating the puncta with cautery. Laser cautery less effective than surgical thermal coagulation.

MECHANISM OF ACTION

1) Provides viscous layer which stabilizes and thickens pre corneal tear film.
2) Prolongs tear film break up time.
3) Keeps ocular surface wet and lubricated.
4) Helps to repair ocular surface damage.
5) Keeps ocular surface smooth.

Polymer based- most commonly used. These are water based formulations with polymers added to enhance viscosity, lubrication, retention time, and stability.

1) Polysaccharides and vinyl derivatives:

Polysaccharides like mucilages, dextrans, and viscoelastic substances and vinyl derivatives are the most common polymers used.

a) Substituted cellulose esters: Methyl cellulose for mild cases.

Hydroxy methyl cellulose, Hydroxy propyl methyl cellulose, Carboxy propyl methyl cellulose. These are longer lasting and adhere to ocular surface

a) Viscoelastic agents: Sodium hyaluronate, Sodium chondroitin sulphate
b) Vinyl derivatives: Polyvinyl alcohol, Polyvinyl Pyrrolidone.

Other ingredients:

2) Electrolytes:

It helps to maintain or lower the osmolarity of artificial tears as compared to natural tears. Some are important for corneal epithelial metabolism like sodium chloride and potassium. Hypotonic tear formulations tend to reduce tear osmolarity and cause relief. HYPOTEARS, THERA TEARS are such formulations.

3)Buffers:

Artificial tears with a pH approaching 8.5 are more comfortable for dry eye patients. Some common buffer systems are phosphate, phosphate-acetate, phosphate-citrate etc

4)Nutrients :

Dextrose, sodium lactate, sodium citrate, vitamins A, B12, C.

5)Preservatives:

They inhibit the growth of microorganisms, by bacteriostatic effect and increases the shelf life of medication. Also helps in increasing corneal penetration of medications.

Various preservatives that are available: Benzalkalanium chloride (most toxic), cholorobutanols, thiomersals, EDTA, sodium perborate.

Complications of tear substitutes with preservatives include pigmentation, irritation, papillary and follicular conjunctivitis, superficial punctate keratitis, epithelial cell exfoliation.

2)Gels:

It is a semi solid formulation tat persists in cul-de-sac for a longer period of time. This decreases the frequency of application and is more effective in relieving the symptoms and signs.

3)Mucolytic agents:

It softens the mucus and make it more fluid. Its available as 5% or 10% acetylcysteine. It has an intracellular effect on goblet cell during mucin formation, facilitating production & improving quality. It is useful in treating patients with corneal filaments and mucous plaques.

4) Serum eye drops:

It is a prepared from autologous or umblical cord serum(20-100%). It is found to be very useful in sjogren's syndrome patients.

5) Artificial tear inserts :

Lacrisert (merck) is a sterile, translucent, water soluble cylindrical rod which is 1.25mm wide and 3.50mm long containing 5mg preservative free hydroxypropyl

cellulose which is placed into inferior fornix. It imbibes water, swells and dissolves. Effect begins after 1 h & remains for 14–24 h, so 1 insert / morning is enough for 1 day. It stabilizes & thickens precorneal tear film.

II) TEAR CONSERVATION

Includes the techniques used to reduce evaporation.

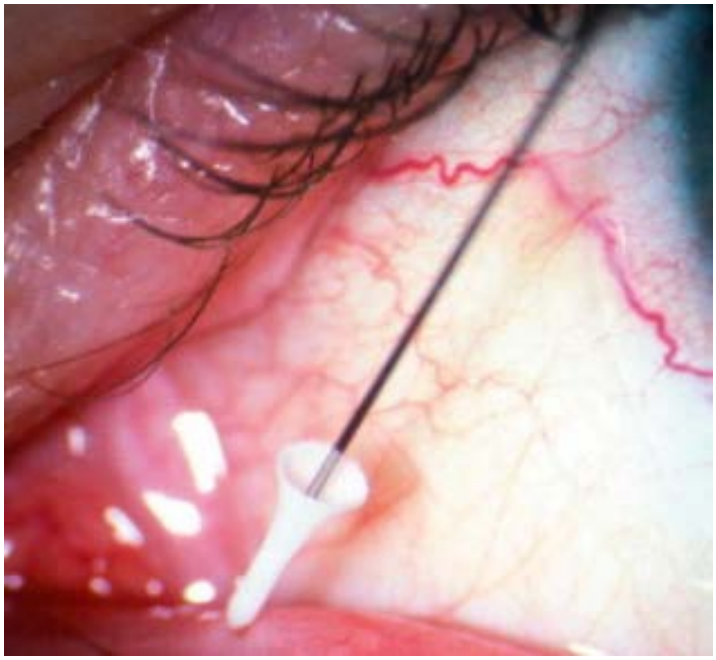
1) Environmental modifications:

By bringing life style changes like humidifiying ambient air by using humidifiers, lowering computer screen below eye level, regular reading breaks, with eyes closed during rest, increasing blink frequency, by avoiding- wind, air conditioning, dry heat, high altitudes, smog, exhaust, tobacco smoke, prolonged computer/ television use, prolonged contact lens wear.

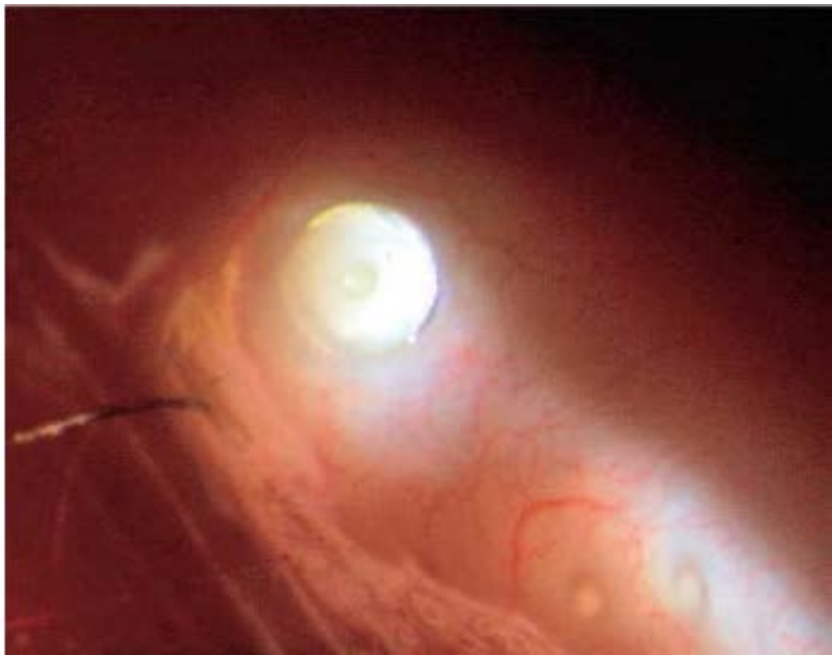
2) Ointments:

Petrolatum, mineral oil, lanolin are the esters of fatty acids with long chain alcohol which serve as lubricants and create a lipid layer retarding evaporation. It is used as a bed time dosage to supplement day time drops and avoided in day time as it can cause blurring of vision.

PUNCTAL PLUG



PUNCTAL PLUG IN PLACE



III) TEAR STIMULATION

Secretagouges

-Diquafosol 3% is a newer agent that acts as a topical secretagogue. P2Y2 purinogenic agonists stimulate secretion of tear fluid and mucin on ocular surface and increase tear film stability.

-Oral cholinergic agonists like pilocarpine(5mg 4 times daily) & cevilemine(30 mg 3 times daily) bind to the muscarinic receptors and stimulate secretion of tears

-Bromhexine

-Rebamipide- newer drug, a mucin secretagouge

IV. Other Management

Systemic medications: Systemic omega-3 fatty acids like fish oil,flax seed oil .It inhibits the synthesis of pro-inflammatory mediators.

Surgeries: Repair of eyelid -Trichiasis, Entropion, Ectropion ,Lateral Tarsorrhaphy, Amniotic membrane transplantation, Submandibular gland transplantation. For cases with very severe dry eye, Keratopreosthesis is the only option to restore vision.

Anti-inflammatory agents:

- **Topical steroids:** Low potency steroids like fluoromethalone, lotepred 0.5% in frequent intervals for 2 weeks is an effective supplementary treatment for acute excerbation. It reduces the ocular inflammation.
- **Topical ciclosporin (0.05%)** When applied twice daily, it can reduce T-cell mediated inflammation of lacrimal tissue and increase the number of goblet cells.
- **Oral tetracyclines:** Given as extended course for 3 months at low dose. It helps in controling blepharitis, meibominitis and reduces the tear levels of inflammatory mediators.

Moisture Chamber Spectacles

Contact lenses: Though contact lens wear exacerbate inflammatory & evaporative effects ,benefits outweigh the side effects. It acts by the fluid trapped behind the lens ,thereby effective by relieving symptoms. HEMA lenses for moderately dry eye, Silicone rubber lenses and Occlusive gas permeable scleral contact lens for extreme dry eye.

Botulinum toxin injection-

To orbicularis muscle at medial canthus, is given to control blepharospasm in severe dry eye. Also reduces tear drainage by limiting the lid movement.

STRATEGY FOR TREATMENT

DEWS guidelines based on earlier international taskforce

Level 1: Mild to moderate symptoms, no signs

Mild to moderate conjuctival signs

Stategy

1) Education & environmental/dietary modifications: importance of compliance

Lifestyle review (importance of blinking, using computer screen below eye level)

Aids for instillation of eye drops

Caution the patient that laser refractive surgery would not be possible

Systemic medication review

Artificial tear substitutes(use of preserved drops come under level 1,non-preserved drops categorized under level 2)

Eyelid therapy: hygiene, lid surgery, tapping of eyelids, swimming goggles, tarsorraphy

Level 2

Moderate to severe symptoms tear film signs, visual signs

Mild corneal punctate staining

Mild conjuctival staining

Strategy:

Non-preserved tear substitutes

Anti-inflammatory agents(topical steroids,omega fatty acids,topical ciclosporin)

Tetracyclines

Punctal plugs

Secretagogues (pilocarpine,cevilemine,rebamipide)

Moisture chamber spectacles

Spectacle side shields

Level 3

Moderate to severe symptoms

Marked corneal punctate staining

Central corneal staining

Filamentary keratitis

Strategy:

Serum eye drops

Contact lenses

Permanent punctal occlusion

Level 4

Severe symptoms

Severe corneal staining and erosions

Conjuctival scarring

Strategy:

Systemic anti-inflammatory agents

Surgery-eyelid surgery, tarsorraphy, salivary gland autotransplantation, mucous membrane/amniotic membrane transplantation.

Table 5: Treatment Recommendations for Dry Eye Disease by Disease Severity Level

Severity Grade	Treatment Recommendations
• Mild	• Education and Environment modifications • Elimination of offending topical and/or systemic medications • Aqueous enhancement: Artificial tear substitutes; gels/ ointments • Eyelid therapy (warm compress and eyelid hygiene) • Treatment for contributing ocular factors such as blepharitis or meibomianitis – e.g., Systemic Tetracyclines
• Moderate	*In addition to above treatments:* • Anti-inflammatory agents (topical cyclosporine and corticosteroids), systemic Omega-3 fatty acids supplements • Punctal plugs • Spectacle side Shields; Moisture chamber goggles
• Other	*In addition to above treatments:* • Systemic cholinergic agonists; Oral pilocarpine. cevimeline • Systemic anti-inflammatory agenis • Mucolytic agents • Autologous serum tears • Contact lenses • Permanent punctal occlusion • Repair of eyelid abnormalities (malpositions or exposure) • Tarsorrhaphy • Mucus membrane, amniotic membrane transplantation

Data from Pflugfelder SC (Chair). Management and Therapy Subcommittee of the International Dry Eye Workshop. Management and Therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye Workshop (2007). *Ocul Surf* 2007;5:174.

DRY EYE CONSENSUS GUIDELINES (DELPHI MODEL) 2006-07

Proposed a new terminology for dry eye- DYSFUNCTIONAL TEAR SYNDROME (DTS). It classified the DTS into 3 major categories and subset of each of these categories are distinctly different from each other in terms of their pathology and the treatment recommendations. The classification was based on the site of lid pathology, anatomical and functional abnormalities.

Classification:

1) With lid margin disease- anterior and posterior
2) Tear distribution problems-conjuctivochalasis, lid ans lash abnormalities, elevated surface lesions, reduced blink rate
3) Without lid margin disease

DTS was classified into 4 levels based on severity of the signs and symptoms. The diagnostic tests were considered secondary.

This study recognised that most of the cases of DTS had an underlying inflammation as causative agent. It also confirmed that patients may move in between the various severity levels, and if left untreated may lead to complications.

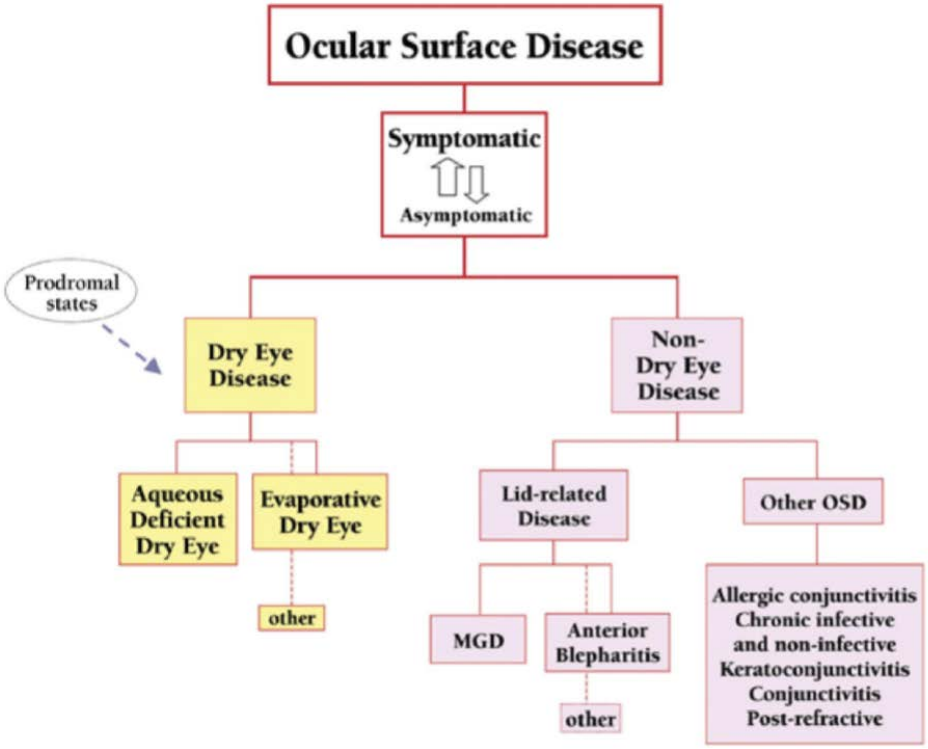
PROGRESSION OF DRY EYE SEVERITY LEVELS	
LEVEL 1	Mild to moderate symptoms ,no signs Mild to moderate conjunctival signs
LEVEL 2	Moderate to severe symptoms Tear film signs,visual signs Mild corneal punctuate staining Conjunctival staining
LEVEL 3	Severe symptoms Marked corneal punctuate staining Central corneal staining Filamentary keratitis
LEVEL 4	Severe symptoms Severe corneal staining,erosions Conjunctaval scarring

DRY EYE TREATMENT CHART				
SEVERITY	1	2	3	4
Symptoms	Mild To Moderate	Moderate To Severe	Severe	Severe
Conjunctival Signs	Mild To Moderate	Staining	Staining	Scarring
Corneal Staining		Mild Punctate Staining	Marked Punctate Staining, Central Staining, Filamentary Keratitis	Severe Staining
Other Signs		Tear Film:Vision Blurring		
TREATMENT OPTIONS				
	-Patient Education -Environmental Modification -Preserved Tears -Control Allergy	-Unpreserved Tears -Gels ,Ointments -Topical Prescription Therapies - Secretagogues -Nutritional Support	-Oral Tetracycline - Punctal Plugs	-Systemic Anti-inflammatory Therapy -Oral Cyclosporin -Acetylcysteine -Moisture Goggles - Surgery(Punctal Cautery)

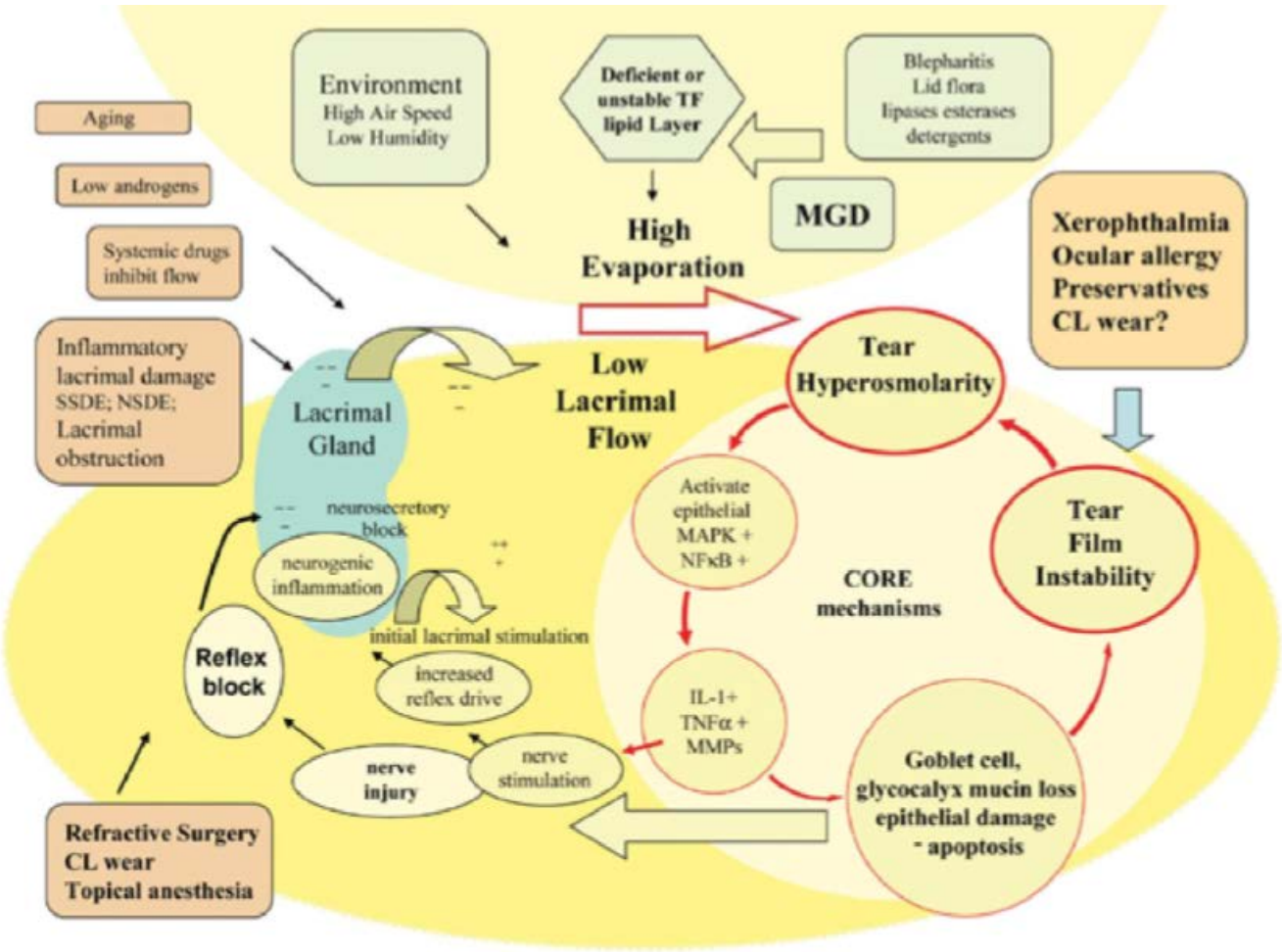
DEWS(Dry Eye Work Shop) Guidelines

DEWS based the revised classification scheme on the updated Triple Classification published in 2005 and the report of the Delphi Panel published in 2006. A three-part classification system was developed.

The first part is etiopathogenic and illustrates the multiple causes of dry eye.



The second is mechanistic and shows how each cause of dry eye may act through a common pathway, and that any form of dry eye can interact with and exacerbate other forms of dry eye as part of a vicious circle.



The third is a scheme based on the severity of dry eye disease, which is expected to provide a rational basis for therapy

TABLE 1

The DEWS Dry Eye Diagnosis Grid* (modified from *The Ocular Surface 2007*)

DRY EYE SEVERITY LEVEL	1	2	3	4
Discomfort, severity, and frequency	Mild/episodic/ environmental stress	Moderate/episodic or chronic/environmental stress or no stress	Severe/frequent or constant without stress	Severe and disabling, constant
Visual symptoms	None or episodic mild fatigue	Annoying and/or activity limiting episodic	Annoying, chronic and/or constant limiting activity	Constant and/or possibly disabling
Lid/meibomian glands	MGD variably present	MGD variably present	Frequent	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Variable	≤ 10	≤ 5	Immediate
Corneal Staining (NEI Scale 0-15)	None to mild	Variable	Central	Severe punctuate erosions
Conjuntival Staining (NEI Scale 0-18)	None to mild	Variable	Moderate to marked	Marked
Schirmer test (no anesthesia) (mm/5 min)	Variable	≤ 10	≤ 5	≤ 2
Recommended management	Patient education, diet modification and lid therapy, artificial tear/gel supplements, environmental control	Add anti-inflammatories, tetracyclines, punctal plugs, moisture chamber spectacles	Add autologous serum, bandage or large-diameter rigid contact lenses, permanent punctual occlusion	Add systemic anti-inflammatory agents, surgical intervention

OSDI QUESTIONNAIRE

It is widely used by ophthalmologists these days to diagnose dry eye disease. This questionnaire being easier to understand to given to the patient themselves to monitor the progress of the disease

Ocular Surface Disease Index© (OSDI©)[2]

Ask your patient the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

HAVE YOU EXPERIENCED ANY OF THE FOLLOWING *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

Subtotal score for answers 1 to 5 (A)

HAVE PROBLEMS WITH YOUR EYES LIMITED YOU IN PERFORMING ANY OF THE FOLLOWING *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

Subtotal score for answers 6 to 9 (B)

HAVE YOUR EYES FELT UNCOMFORTABLE IN ANY OF THE FOLLOWING SITUATIONS *DURING THE LAST WEEK*:

	All of the time	Most of the time	Half of the time	Some of the time	None of the time	
10. Windy conditions?	4	3	2	1	0	N/A
11. Places or areas with low humidity (very dry)?	4	3	2	1	0	N/A
12. Areas that are air conditioned?	4	3	2	1	0	N/A

Subtotal score for answers 10 to 12 (C)

ADD SUBTOTALS A, B, AND C TO OBTAIN D (D = SUM OF SCORES FOR ALL QUESTIONS ANSWERED) (D)

TOTAL NUMBER OF QUESTIONS ANSWERED (DO NOT INCLUDE QUESTIONS ANSWERED N/A) (E)

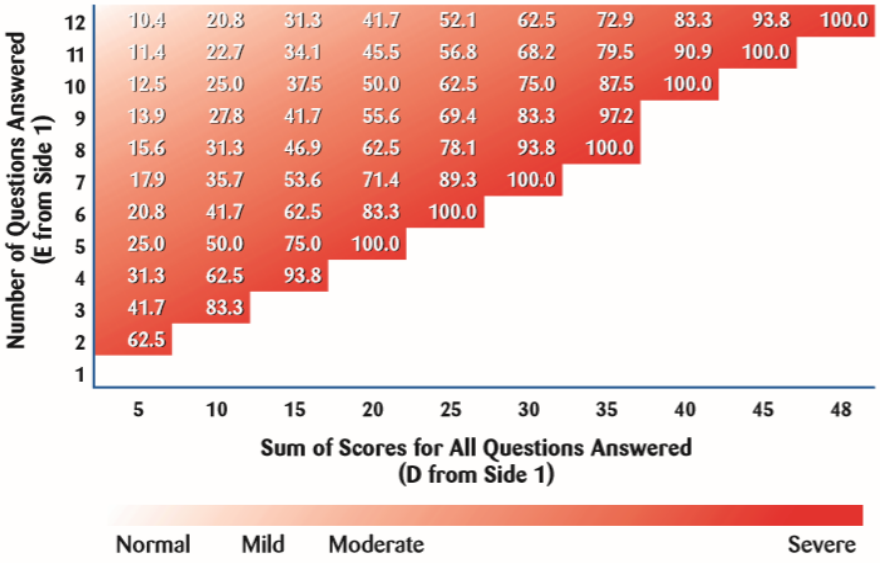
Please turn over the questionnaire to calculate the patient's final OSDI© score.

Evaluating the OSDI© Score[1]

The OSDI© is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI© is a valid and reliable instrument for measuring dry eye disease severity (normal, mild to moderate, and severe) and effect on vision-related function.

Assessing Your Patient's Dry Eye Disease[1,2]

Use your answers D and E from Side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.*
Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



*Values to determine dry eye disease severity calculated using the OSDI© formula:

$$\text{OSDI}^{©} = \frac{(\text{sum of scores}) \times 25}{(\#\text{ of questions answered})}$$

Patient's Name: _____ **Date:** _____

How long has the patient experienced dry eye? _____

Eye Care Professional's Comments: _____

ANTI-PSYCHOTIC AGENTS

CLASSIFICATION:

1) PHENOTHIAZINES:

Aliphatic side chain	-	Chlorpromazine, Triflupromazine
Piperidine side chain	-	Trifluoperazine
Piperazine side chain	-	Trifluoperazine, Fluphenazine
2) BUTYROPHENONES		Haloperidol, trifluperidol, Droperidol, Penfluridol
3) THIOXANTHINES	-	Thiothixene, Flupenthixol
4) OTHER HETERO CYCLICS	-	Pimozide, Loxapine
5) ATYPICAL NEUROLEPTICS	-	Clozapine, Olanzapine, Risperidone

PHARMACOLOGICAL ACTIONS:

1) CNS- In normal individuals, it causes paucity of thought, indifference to surroundings, psychomotor slowing, tendency to sleep off from which he is easily arousabe. Spontaneous movements are minimised. This is known as NEUROLEPTIC SYNDROME.

In psychotic individuals, it reduces irrational behaviour, agitation and aggressiveness. Hyperactivity, hallucinations and delusions suppressed.

Aliphatic and piperidine side chains have low potency but more sedative action. Extrapyramidal side effects and anti-emetic effects are related to anti-psychotic effects least with Thioridazine.

Mechanism of action- D2(Dopamine receptors) blocking effect in the limbic system and mesocortical area is responsible for anti-psychotic effect except clozapine. Clozapine has 5HT2 and alpha1 blocking action and D4 blocking effect as well. Dopaminergic blockade in basalganglia is responsible for extra-pyramidal effects and in CTZ for anti-emetic action.

c) ANS:

Alpha 1 blocking effect-

CPZ=triflupromaizne>thioridazine>fluphenazine>haloperidol>trifluoperazine>

clonazapine>pimozide

Anticholinergic effect-thioridazine>chlorpromazine>

trifluprомazine>trifluperazine=haloperidol.

H1, 5HT blocking effect-phenothiazines.

3) LOCAL ANAESTHETIC- Chlorpromazine has potent local anaesthetic effect.

4) CVS-Hypotension due to central and peripheral effect on sympathetic tone. High doses of CPZ depresses heart. However,it has some membrane stabilizing effect.

5) SKELETAL MUSCLE- reduces some types of spasticity due to action in basal ganglia and medulla.

6) ENDOCRINE- increases prolactin levels by blocking dopamine receptors in pituitary lactotrophes. Reduces onadotrophin secretion, ACTH, GH, ADH release.

ADVERSE EFFECTS

BASED ON PHARMACOLOGICAL ACTIONS(DOSE RELATED)

1) CNS- Lethargy, drowsiness, confusion and weight gain, aggravation of seizures in epileptic patients.

2) ADRENERGIC BLOCKING EFFECTS-postural hypotension, palpitation, inhibition of ejaculataion.

3) ANTI-CHOLINERGIC EFFECTS-dry mouth, constipation, urinary hesitancy in elderly males, blurring of vision. Clonazepine may induce hypersalivation due to centra action.

4) ENDOCRINE-amenorrhoea, infertility, gynaecomastia, galactorrhoea

5) EXTRAPYRAMIDAL SIDE EFFECTS-Parkinsonism, Tardive dyskinesia, Acute muscular dystonias, akathisia, Malignant neuroleptic syndrome,.

6)MISCELLANEOUS- weight gain, bluish pigmentation of exposed skin, corneal and lenticular degenrations, retinal degeneration (more with thioridazine). Cardiac arrhythmias, myocarditis.

HYPERSENSITIVITY REACTIONS

1) Cholestatic jaundice

2) Skin rashes, urticaria, contact dermatitis, photosensitivity & Agranulocytosis

USES

1) PSYCHOSES

Schizophrenia- used primarily in functional psychoses. They control positive symptoms of schizophrenia better than negative symptoms. They tend to restore cognitive, affective and motor disturbances.

- In agitative, combative and violent patients-CPZ, triflupromazine, haloperidol.
- Withdrawn and apathetic-trifluperazine, fluphenazine
- Negative symptoms and resistant cases-clozapine, olanzapine
- Mood elevation, hypomania-haloperidol, fluphenazine.
- In chronic schizophrenia, effect may be seen after 2-4 months of therapy.
- Mania – in acute episode, i.m. injections of lithium and carbamazapine can be given, whichcan be tapered later.
- Organic brain syndromes

2) ANXIETY- the patients not responding to anxiolytics or have a psychotic basis for anxiety may be treated with this class of drugs.

3) ANTI-EMETIC- for drug and disease induced vomiting at low doses. But ineffective in motion sickness.

4) OTHER USES :

- To potentiate hypnotics, analgesics, anaethsetics
- Intractable hiccough- responds to parentral CPZ
- Tetanus-CPZ is used for muscle relaxation.
- Alcohol hallucinosis, huntington’s disease, gilles de la tourette’s syndrome.

OCULAR SIDE EFFECTS OF ANTI-PSYCHOTICS

Psychoactive drugs are prescribed frequently for a variety of conditions to alter mood and emotional status. Whether it's short-term use of an antidepressant or a lifelong reliance on an anti-schizophrenia drug, most of the people will meet the criteria for a DSM-IV and -V disorder at some point in their lifetime. Because of chronicity of neuroleptic usage, they show a lot of side effects Liver is the most common drug to show drug toxicity, followed by eye.

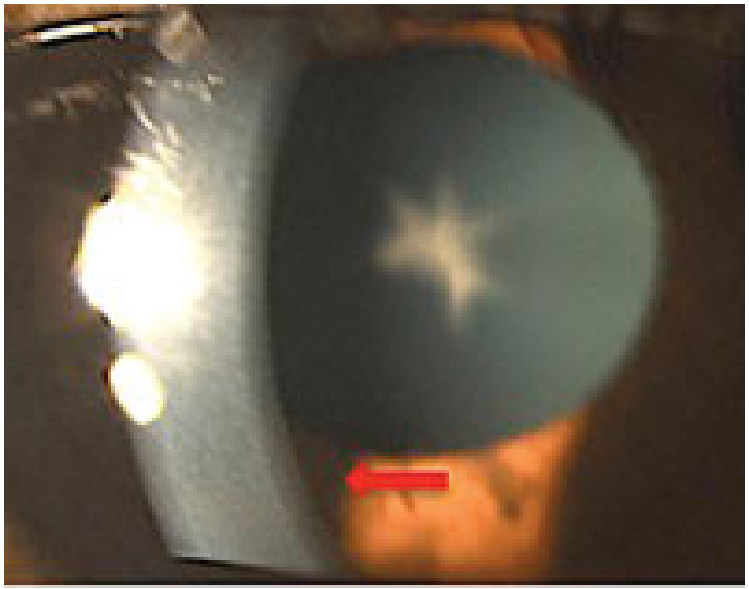
1) Ocular Surface

Drug toxicity to the ocular surface can manifest in the form of corneal edema, epithelial keratopathy, and altered tear film.[11]

Phenothiazines can cause phototoxic lysis of the corneal endothelium which in turn is linked to the total dosage of medication. This can lead to impaired endothelial pump function, causing severe corneal edema and consequent visual effects.[12]

Chlorpromazine has been found to cause corneal epithelial keratopathy.[11]It has a distinctive pattern of fine streaks or swirling lines in the epithelium. This has been linked to high dosages (>2g/day) of the drug.[11] This causes minimal visual consequences and usually regresses with dose tapering. An innocuous, subtle, diffuse yellowish-brown granular deposits in the endothelium, Descemet

GRANULAR ENDOTHELIAL DEPOSITS



membrane and deep stroma occurring only in exposed cornea of the interpalpebral fissure is also common.

Psychiatric medications can also alter the quantity and quality of tears. These medications due to their anticholinergic effects tend to alter the tear film.

Clozapine, an atypical antipsychotic medication, exhibits anticholinergic side effects by blocking muscarinic and nicotinic receptors, and muscarinic-3 receptors in the conjunctiva and lacrimal gland as well.[10]This leads to decreased mucous and aqueous secretion.[10] Persistent tear film instability can lead to morphological and biomechanical changes at the cellular level, ultimately affecting the ocular surface and vision.[11] Prompt lubrication and use of tear rehabilitating agents as cyclosporine can prevent desiccation.

2) Ocular Pigmentation

Chlorpromazine is more likely to cause pigmentary changes compared to clozapine.[4,13,14] Ocular pigmentation following drug toxicity can be divided into two groups: pigmentation of the skin, conjunctiva, cornea or lens and pigmentary retinopathy.[13,14] The first may cause minimal to no changes in vision, while pigmentary retinopathy may lead to irreversible degenerative retinopathy.

Chlorpromazine is found to accumulate in the skin of the lids, conjunctiva, posterior corneal stroma, lens and uvea.[4,13,14] As it is phototoxic, it is postulated that photosensitization of the tissue proteins occurs in areas of sun exposure after accumulation of the drug in these tissues.[13,14] Protective dark goggles and reduced exposure to sun ,while on the medication is recommended for these patients. Although these pigmentary changes are not that common with clozapine, there have been reports with a handful of cases.

3) Uveal tissue

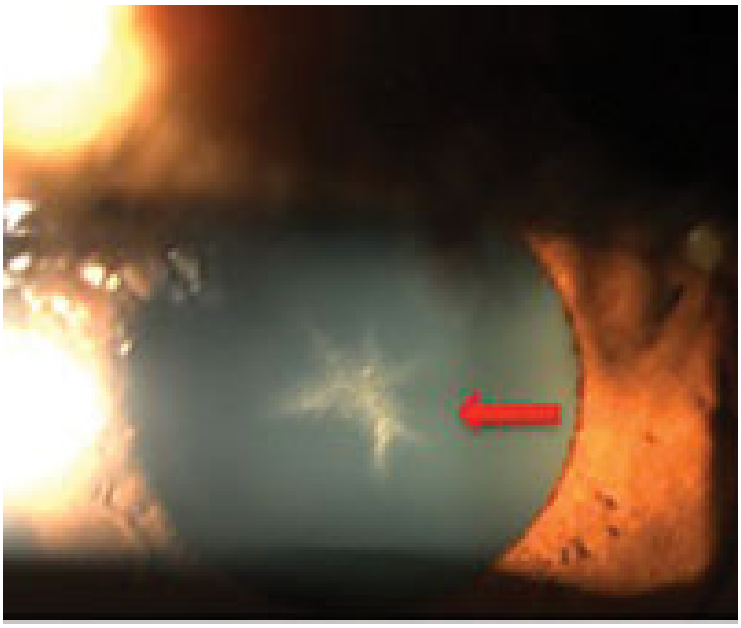
Antipsychotics with a strong anticholinergic and/or antiadrenergic effects (like chlorpromazine and fluphenazine) can cause mydriasis and cycloplegia. Due to this, there is a weakened accommodation leading to blurring of vision.

4) Lenticular Opacities and Cataracts

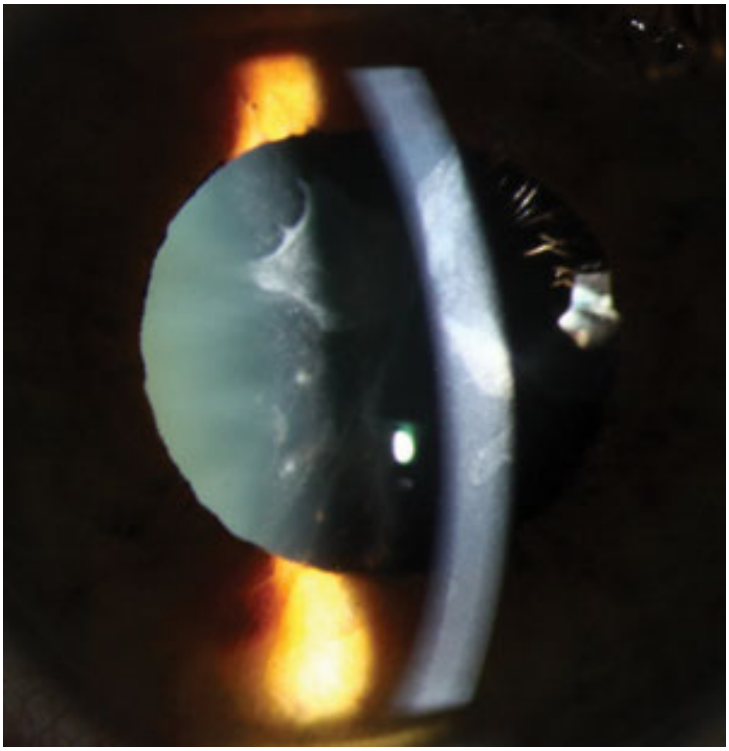
Cataracts secondary to these medications are rarely bilateral and usually asymmetric.[15]This may be due to unequal deposition of medication in the lens. Additionally, atypical antipsychotics can cause metabolic syndrome, hyperglycemic status in these patients can cause an early diabetic cataract formation.[15]

Phenothiazines are the most common antipsychotic agents that can lead to formation of lenticular opacities.[4,7,8] There is a deposition of fine, stellate, yellowish-brown granules on the anterior lens capsule in the pupillary area in 50% of patients who have received a cumulative dose of 1000 g. The deposits persist despite discontinuation of the drug. The normal daily dose is 75–300 mg. The corneal pigmentation occurs in conjuction to anterior subcapsular pigment, which shows a link to alterations in the aqueous humor.[15,16] Phototoxicity is thought to be a potential mechanism of action, although an alternate explanation can be lens discoloration. In certain cases, endogenous melanin in the eye may trap free radicals produced by psychotropic medications, which shows up as lens discoloration.[15,16] These opacities may not reverse with cessation of the medication, however any visual disturbance due to it will vary depending on the duration of exposure and degree of damage.

ANTERIOR SUB-CAPSULAR DEPOSIT



ASYMMERTRICAL LENTICULAR OPACITIES



5) IOP and Angle Closure Glaucoma

Typical antipsychotics having anticholinergic effects can cause an acute angle closure with pupillary block in patients with anatomically narrow angles.[8] The mechanism is believed to be drug-induced mydriasis in an already crowded angle. Thus, these drugs should be prescribed cautiously in patients with already narrow angles.

6) Retinopathy

Ocular pigmentation caused by **phenothiazines** as thioridazine and chlorpromazine, can occur in the retina. The risk with thioridazine is based on large daily doses of >800 mg/day (Normal daily dose is 150–600 mg) , while the risk with chlorpromazine is related to daily dosage and duration of use.[4,8,24] Pigment gets deposited from the peripheral to central retina giving rise to a Salt and Pepper pigmentary disturbance.[24] A plaque-like pigmentation and focal loss of the RPE and choriocapillaris which is later followed by diffuse loss of the RPE and choriocapillaris as the disease progresses. It has been postulated that phototoxic stress causes peripheral vision loss, nyctalopia, permanent vision loss and ultimately blindness as damage progresses.[23] Early detection and intervention can prevent permanent visual damages.

PIGMENTARY RETINOPATHY

7) Ocular Motility Disorders

Oculogyric crisis caused by dystonia, occurs due to involuntary contractions of extraocular muscles. This can cause gaze paralysis which may be painful and even life-threatening if systemic muscles get involved.[5] The etiology is believed to be dopamine receptor blockage along with other causes.[6,8] Treatment consists of anticholinergic agents (intramuscular benzatropine) and antihistamines (diphenhydramine) and can rapidly reverse the symptoms.[4,6,8]

8) Impaired Sensory Perception

Changes to color vision and contrast sensitivity has been noted with psychiatric medications. Regular color vision and contrast sensitivity testing should be done in these patients.

9) Metabolic and Cerebrovascular Implications

Although its proved that newer antipsychotics have safer toxicology profiles as compared to typical antipsychotics, newer medications can still cause metabolic syndrome. Impaired glucose metabolism, exacerbation of existing diabetes, induction of Type 2 diabetes and diabetic ketoacidosis have been linked to antipsychotic medications.[15,33]

Therefore, we should routinely screen for diabetic retinopathy in patients on chlorpromazine, clozapine and olanzapine.[15,33]

Lastly, there has been found to be a increased risk of cerebrovascular events in elderly patients with dementia who are on antipsychotic medications.[33] Typical antipsychotic agents have been associated with a higher risk of cerebrovascular accidents than that with atypical agents.

PART II

AIM

The aim of the study is to find out any disturbance in tear film due to chronic usage of Anti-psychotic medications in patients attending the Psychiatry OPD, Govt Stanley Medical College and Hospital .

1) To determine the prevalence of dry eye disease in patients on chronic anti-psychotic therapy.

2) To determine the association between duration of therapy and dry eye disease.

3) To determine the association of poly-pharmacy with dry eye disease in these patients.

MATERIALS AND METHODS

It is a cross sectional observational study undertaken on 200 eyes of 100 patients who were on chronic anti-psychotic therapy attending the Psychiatry OPD. Out of 100 patients, 65 patients were male, rest 35 were females. 76 patients were on treatment for schizophrenia, 15 had Delusional disorder and 9 had Psychoses-not specified otherwise.

Study period was from 2015-2016

INCLUSION CRITERIA:

- Patients on Anti-psychotic medications for more than 2 years.

EXCLUSION CRITERIA:

- Patients on Anti-psychotic medications for less than 2 years.
- Patients who had an acute episode of the disease.
- Patients on other medications along with Anti-psychotics.
- Patients with other ocular morbidities which can affect tear film.
- Other systemic diseases.

The importance of ocular examination was thoroughly explained to the patients and their caretaker in their own language.

Consent from the patients and their caretakers was obtained in their own language from all those who were willing to take part in the study.

Any photographic records of the lesions were taken only if the patient consented for the same.

Literature of approval attached.

History regarding Anti-psychotic drug usage, its dosage and duration was obtained from the patients and care-takers.

OCULAR EXAMINATION WAS DONE AS FOLLOWS:

- Ocular history
- Ocular examination included:
- Best corrected visual acuity by Snellens Chart
- Slit lamp examination & dilated fundus examination -90D and 20D

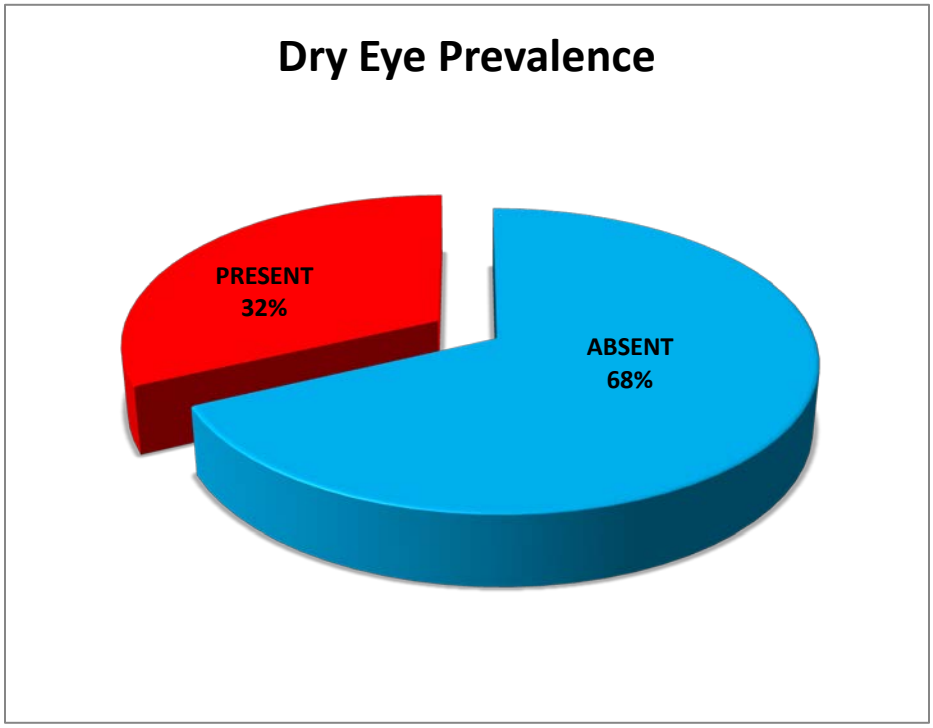
DRY EYE EVALUATION:

- Schrimer’s 1 test:
- Tear film height:
- Tear film break up time:
- Fluorescein staining :

RESULTS AND DISCUSSION

32 out of 100 patients on chronic anti-psychotic therapy had dry eye disease.

17 (53.13%) out of these 32 patients had symptoms suggestive of dry eye disease.

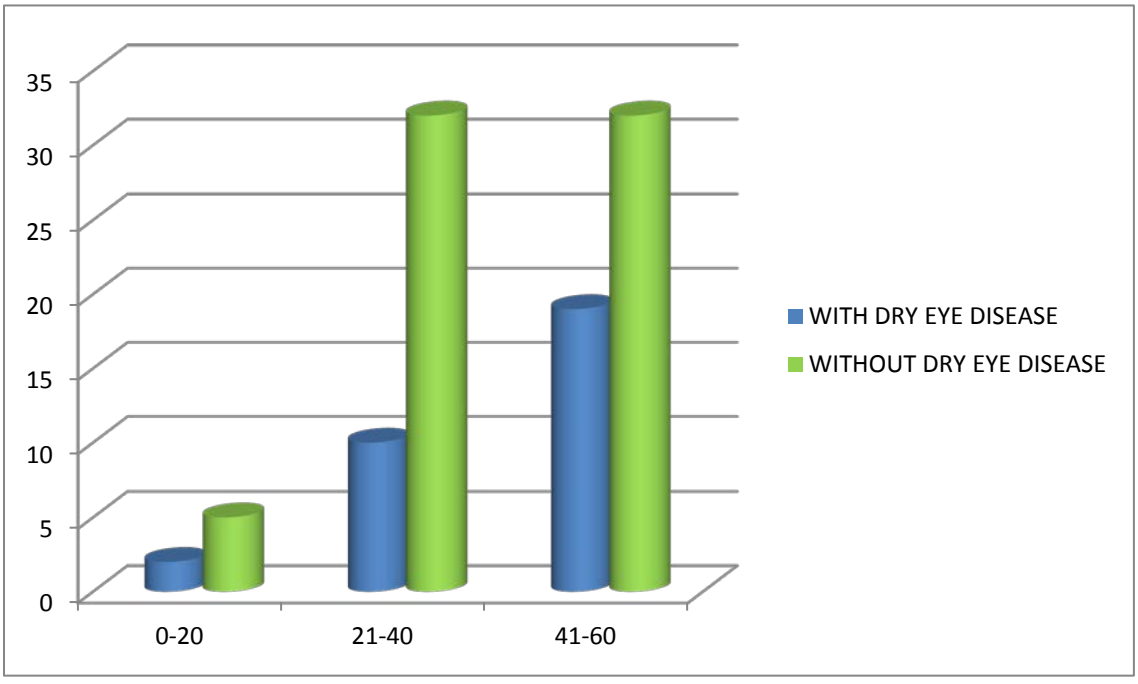


1) AGE DISTRIBUTION:

AGE GROUPS	NUMBER OF PATIENTS WITH DRY EYE DISEASE	NUMBER OF EYES WITH DRY EYE DISEASE
< 20	2	4 (6.7%)
21-40	10	19 (32.2%)
41-60	19	36 (61.01%)
TOTAL	32	59

Most of the patients with dry eye disease belonged to the age group of 41-60 years constituting 61% of total eyes with dry eye disease.

AGE-WISE DISTRIBUTION OF DRY EYE DISEASE

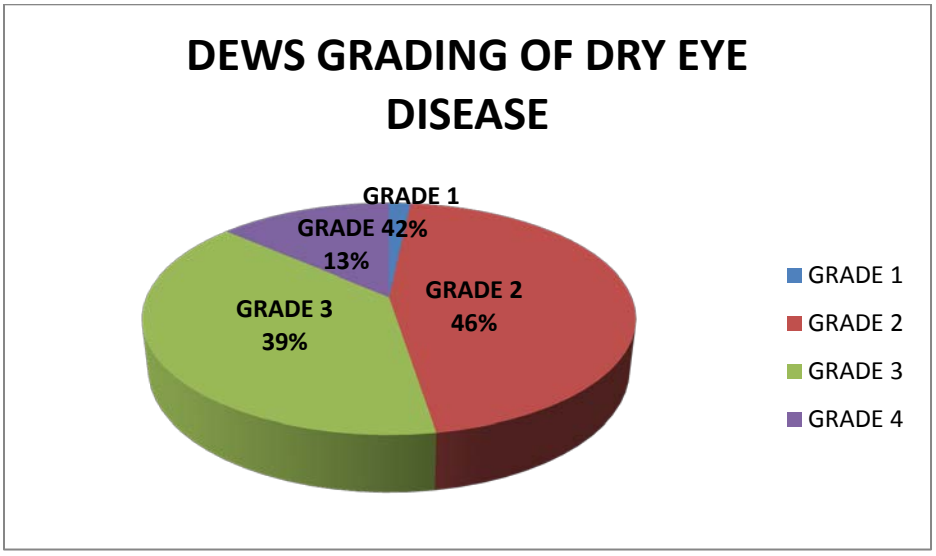


2) GRADING OF DRY EYE DISEASE:

59 out of 200 eyes had dry eye disease. 3 patients out of 32 had unilateral dry eye disease.

DEWS SEVERITY GRADING	NUMBER OF EYES
1	1 (1.6%)
2	27 (45.76%)
3	23 (38.98%)
4	8 (13.55%)
TOTAL	59

27(45.7%) eyes out of 59 eyes diagnosed with dry eye had Grade 2 dry eye disease.

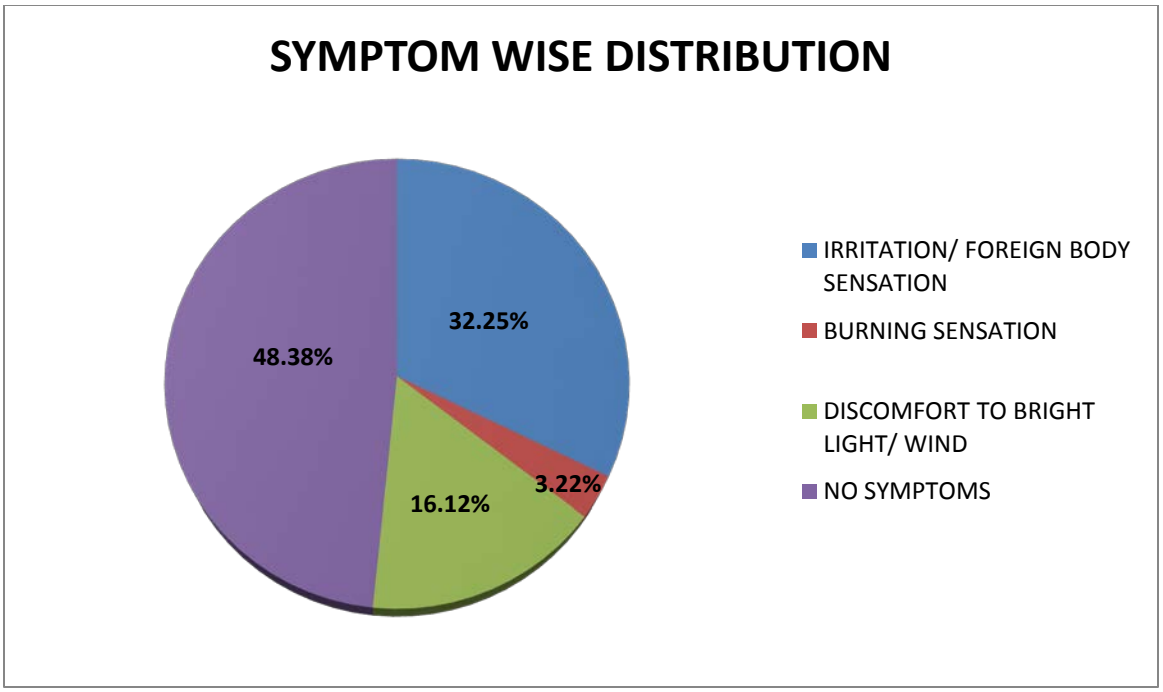


2) SYMPTOMS

SYMPTOMS	NUMBER OF PATIENTS WITH DRY EYE
Irritation/ Foreign Body Sensation	10 (31.25%)
Burning Sensation	2 (6.25%)
Discomfort To Bright Light/ Wind	5 (15.62%)
No Symptoms	15 (46.87%)
TOTAL	32

17 (53.13%) out of 32 patients with dry eye disease had symptoms. Considering this, we should pay importance to their symptoms and evaluate them further objectively.

15 out of 32 did not have any complaints. As most of the patients were in Grade 3 dry eye disease category, we should definitely evaluate these patients even if they are asymptomatic.



3) TEAR FILM MENISCUS HEIGHT

TEAR FILM MENISCUS HEIGHT	NUMBER OF EYES WITH DRY EYE
Abnormal	55 (93.2%)
Normal	4 (6.8%)
Total	59

Tear film height was abnormal in 55(93.2%) out of 59 eyes with dry eye disease.

4) CONJUNCTIVAL INJECTION

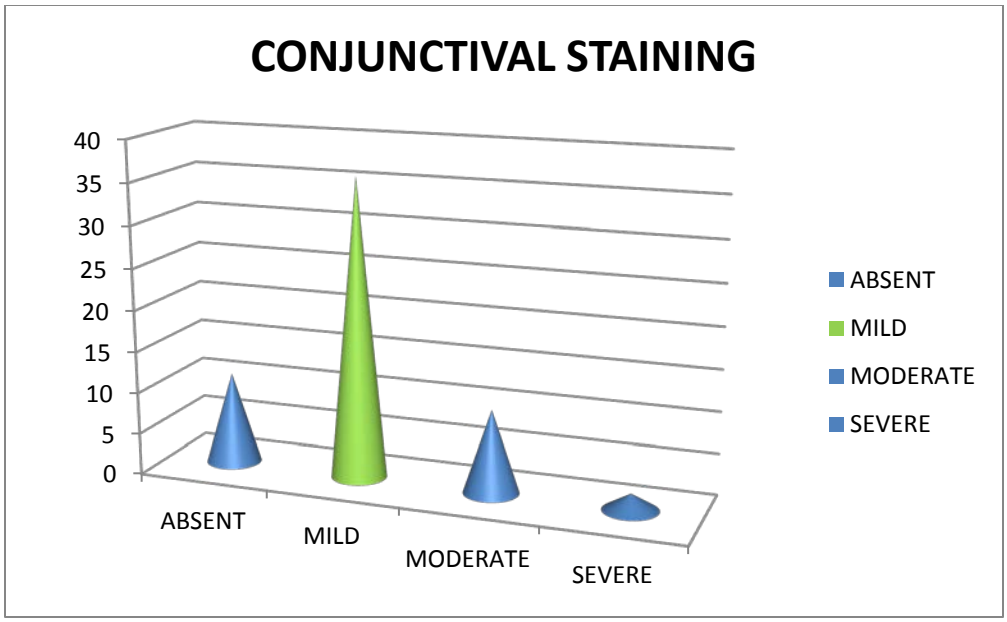
CONJUNCTIVAL INJECTION	NUMBER OF EYES WITH DRY EYE
Absent	47 (79.66%)
Present	12 (20.33%)
Total	59

Conjunctival injection was absent in 47 out of 59 eyes that constitutes nearly 79.66% of positive cases.

5) CONJUNCTIVAL STAINING

CONJUNCTIVAL STAINING	NUMBER OF EYES WITH DRY EYE
Absent	11 (18.64%)
Mild	36 (61.01%)
Moderate	10 (16.94%)
Severe	2 (0.33%)
Total	59

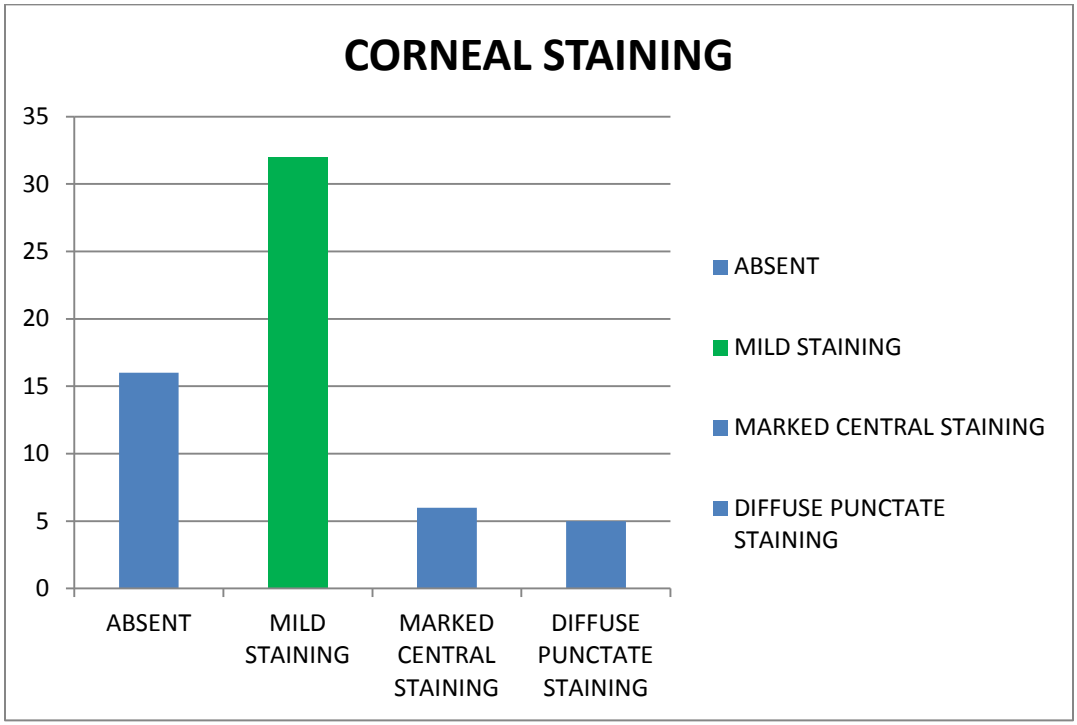
Conjunctival staining with fluorescein was positive in 48 (81.64%) eyes out of 59 diagnosed with dry eye disease.



6) CORNEAL STAINING

CORNEAL STAINING	NUMBER OF EYES WITH DRY EYE
Absent	16 (27.11%)
Mild Staining	32 (54.3%)
Marked Central Staining	6 (1.01%)
Diffuse Punctate Staining	5 (0.84%)
Total	59

Nearly 43(72.89%) out of 59 eyes with dry eye showed corneal staining with fluorescein. Most of the patients had mild corneal staining.



6) TEAR FILM BREAK UP TIME

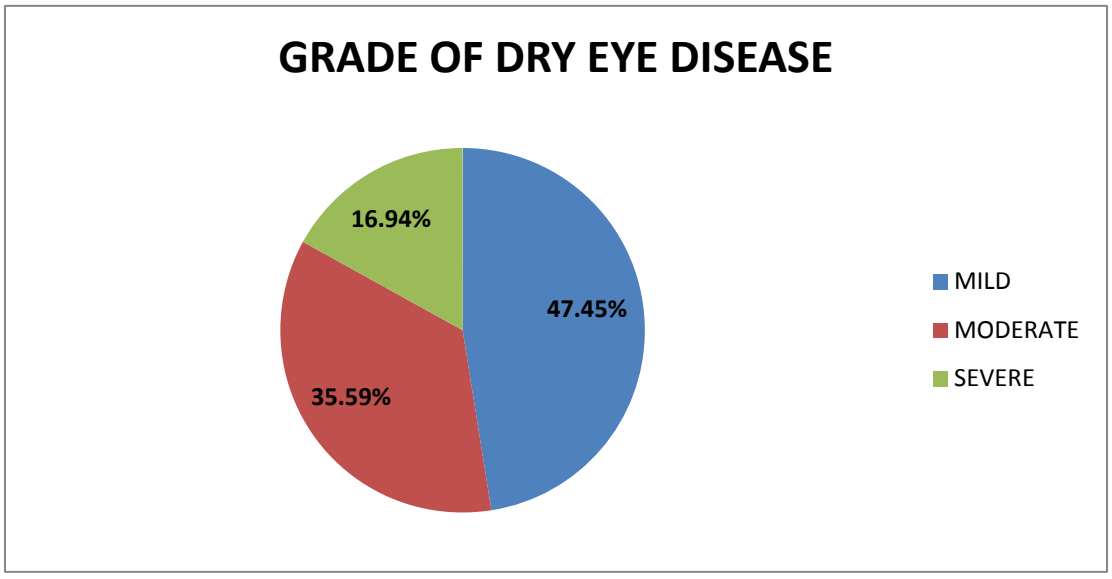
TBUT	NUMBER OF EYES WITH DRY EYE
Abnormal	38 (64.4%)
Normal	21 (35.6%)

38 (64.4%) out of 59 eyes with dry eye disease had abnormal tear film break up time.

7) SCHIRMER'S TEST 1

SCHIRMER'S TEST 1(in mm Hg)	GRADE OF DRY EYE DISEASE	NUMBER OF EYES WITH DRY EYE
6-10	Mild	28 (47.45%)
3-5	Moderate	21 (35.59%)
0-2	Severe	10 (16.94%)
Total		59

Most of the patients had mild dry eye disease, 28 (47.45%) out of 59 eyes.



8) DRUG WISE DISTRIBUTION OF DISEASE:

The most commonly used Anti-Psychotic drugs in our setup is Chlorpromazine, Haloperidol and Risperidone.

Chlorpromazine and Haloperidol are the Typical Anti-Psychotic agents, while Risperidone falls in a relatively newer category of Atypical Anti-psychotic agents.

Of the 100 patients evaluated, 20 were on Chlorpromazine, 23 on Haloperidol and 16 on Risperidone.

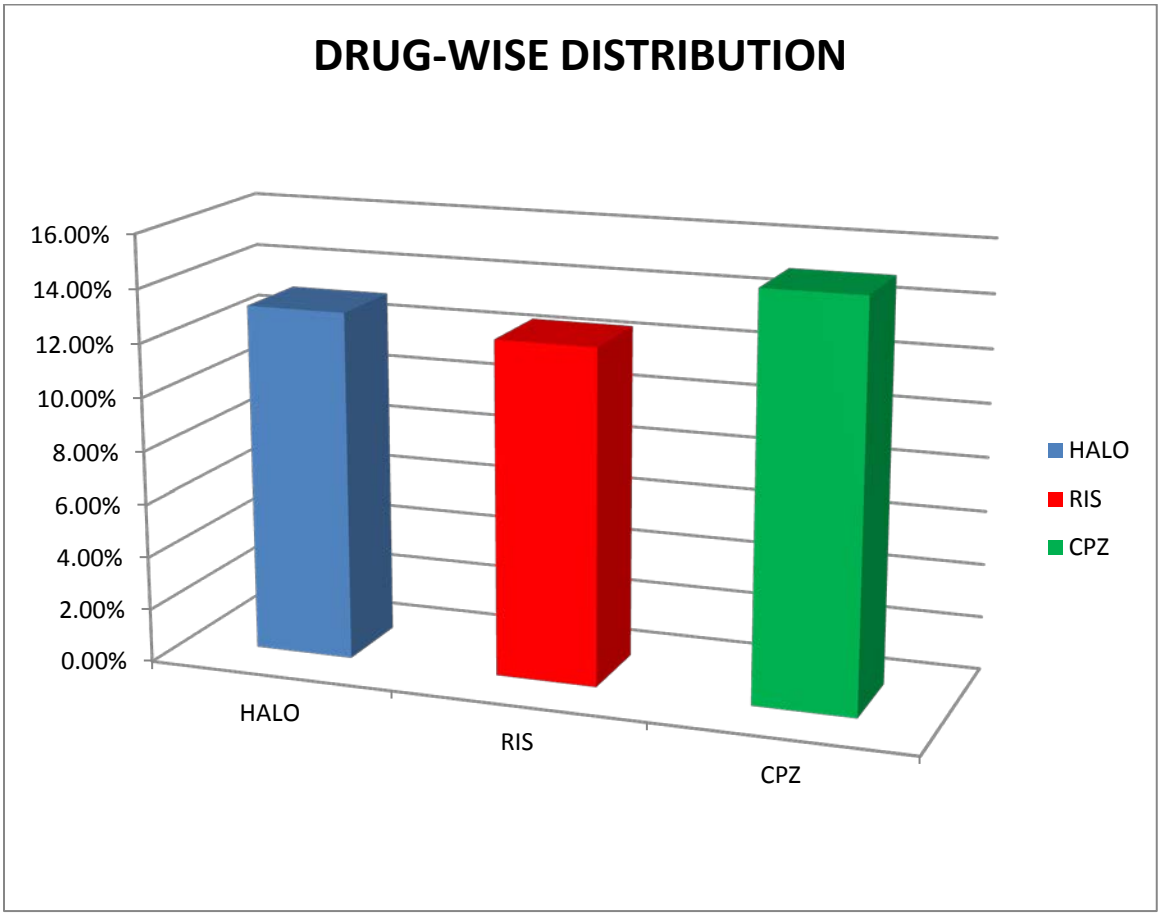
Out of 20 patients who were on Chlorpromazine , 3 (15%) had dry eye disease.

Of the 16 patients on Risperidone , 2 (12.5%)patients had dry eye disease. And Out of 23 patients who were on Haloperidol, 3(13.04%) patients had dry eye disease.

DRUG	DRY EYE DISEASE		TOTAL NO OF EYES
	PRESENT	ABSENT	
Haloperidol	6 (13.05%)	40(86.95%)	46
Risperidone	4(12.5%)	28(87.5%)	32
Chlorpromazine	3(15%)	17(85%)	20
Total	13	85	98

On comparison, the prevalence of dry eye disease showed following order: Chlorpromazine > Haloperidol> Risperidone.

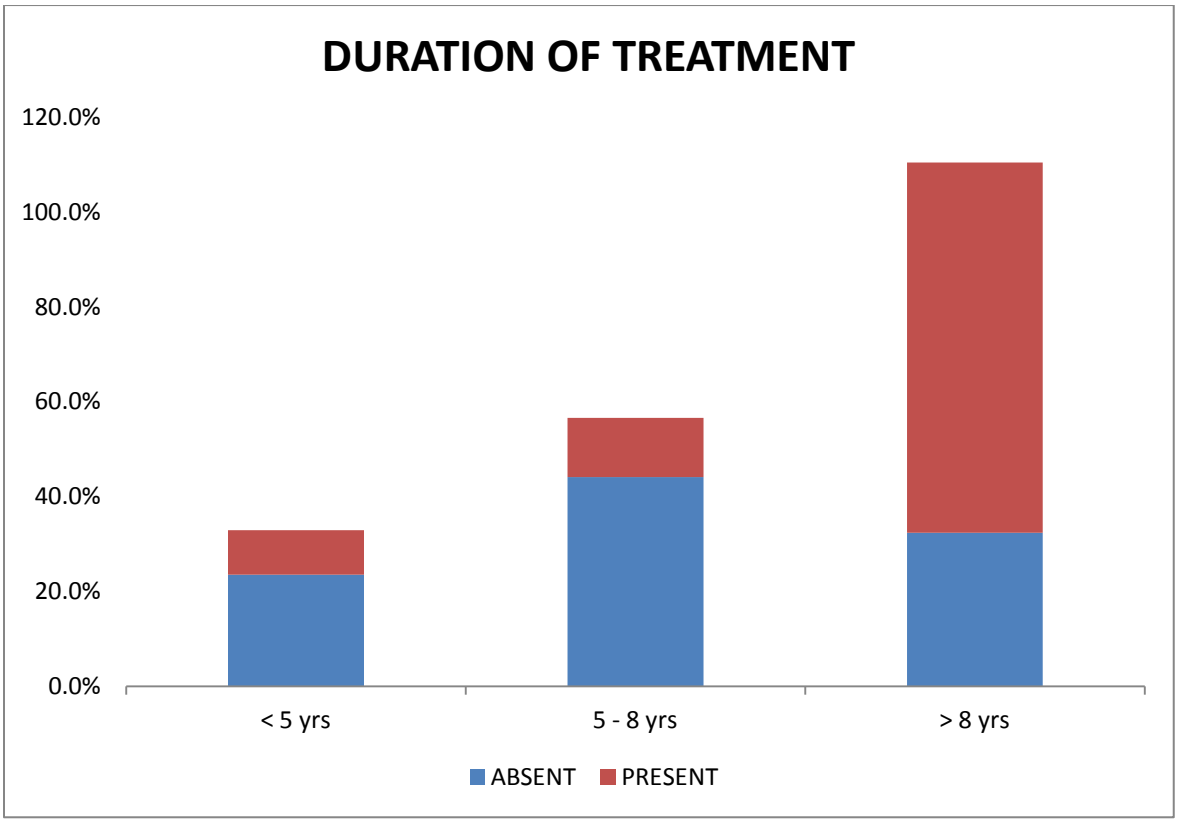
43 patients out of 100 were on Typical anti-psychotics. Of these, 6 (13.95%) patients had dry eye disease. Of the 16 patients on Atypical anti-psychotics, 2 (12.5%) had dry eye indicating more prevalence of dry eye disease in patients on Typical Anti-psychotics than on Atypical agents.



9) DURATION OF DRUG THERAPY

DURATION	DRY EYE DISEASE		TOTAL
	PRESENT	ABSENT	
<5 Years	3 (9.4%)	16 (23.5%)	19
5-8 Years	4 (12.5%)	30 (44.1%)	34
>8 Years	25 78.1%)	22 (32.4%)	47
Total	32	68	100

Nearly 78% of the patients found to have dry eye disease were on treatment with anti-psychotic agents for more than 8 years.



Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	18.392a	2	.000
Likelihood Ratio	19.205	2	.000
Linear-by-Linear Association	13.302	1	.000
N of Valid Cases	100		

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 6.08.

p value is <0.01, proving that the association between the duration of treatment and dry eye disease is significant.

10) MONO-PHARMACY VS POLY-PHARMACY:

Of the 100 patients, 60 were on mono drug therapy. Rest 40 were on multi-drug therapy.

In the Multi-drug group, a combination of Haloperidol, Chlorpromazine and Risperidone was used by 4 patients, 26 patients were on Haloperidol and Chlorpromazine and 10 patients were on Risperidone and Chlorpromazine combination.

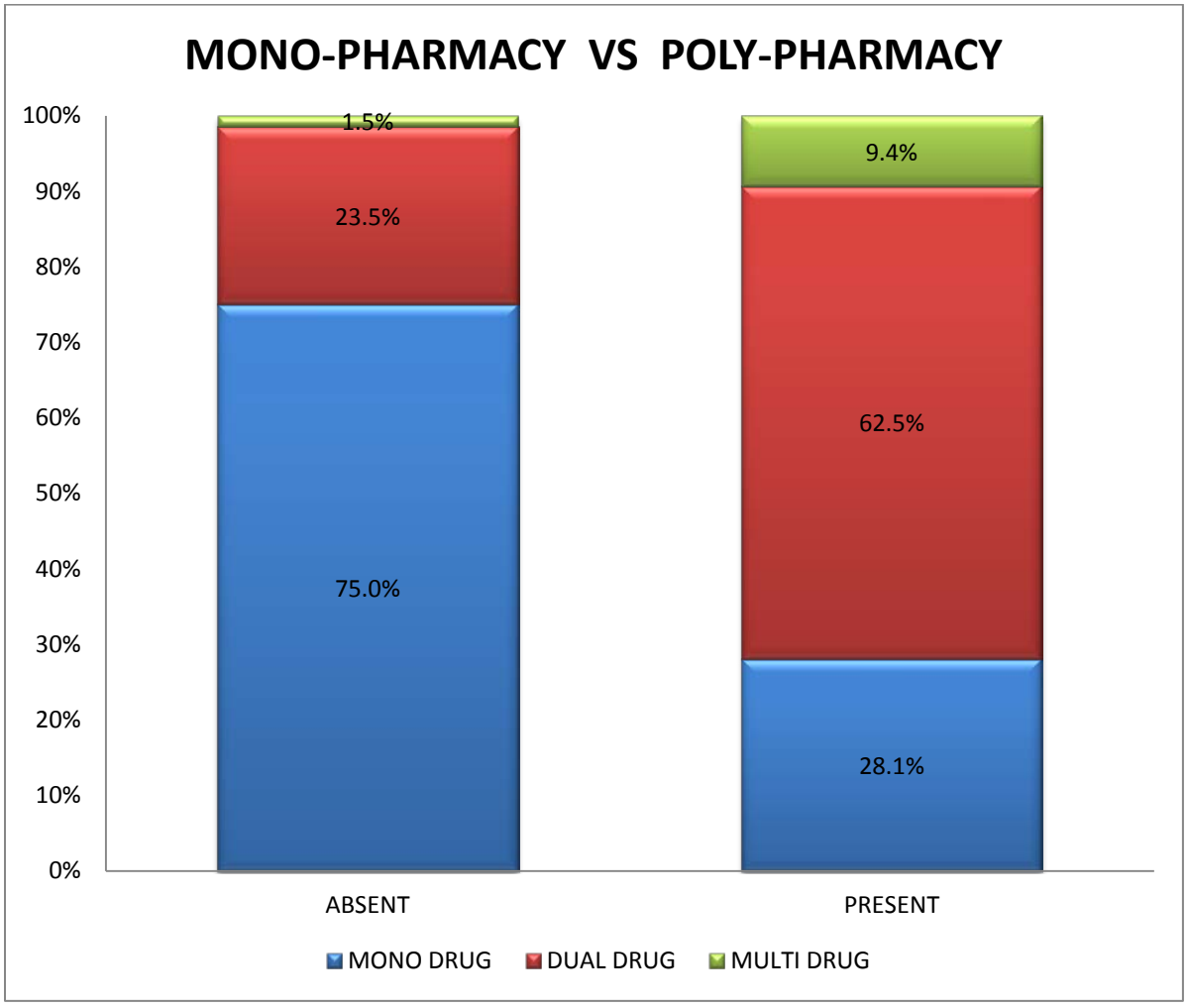
TREATMENT	DRY EYE DISEASE		TOTAL
	ABSENT	PRESENT	
Mono Drug Therapy	51 (75%)	9(28.1%)	60
Dual Drug Therapy	16 (23.5%)	20 (62.5%)	36
Multi Drug Therapy	1 (1.5%)	3 (9.4%)	4
Total	68	32	100

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	20.547[a]	2	.0005
Likelihood Ratio	20.689	2	.000
Linear-by-Linear Association	19.805	1	.000
N of Valid Cases	100		

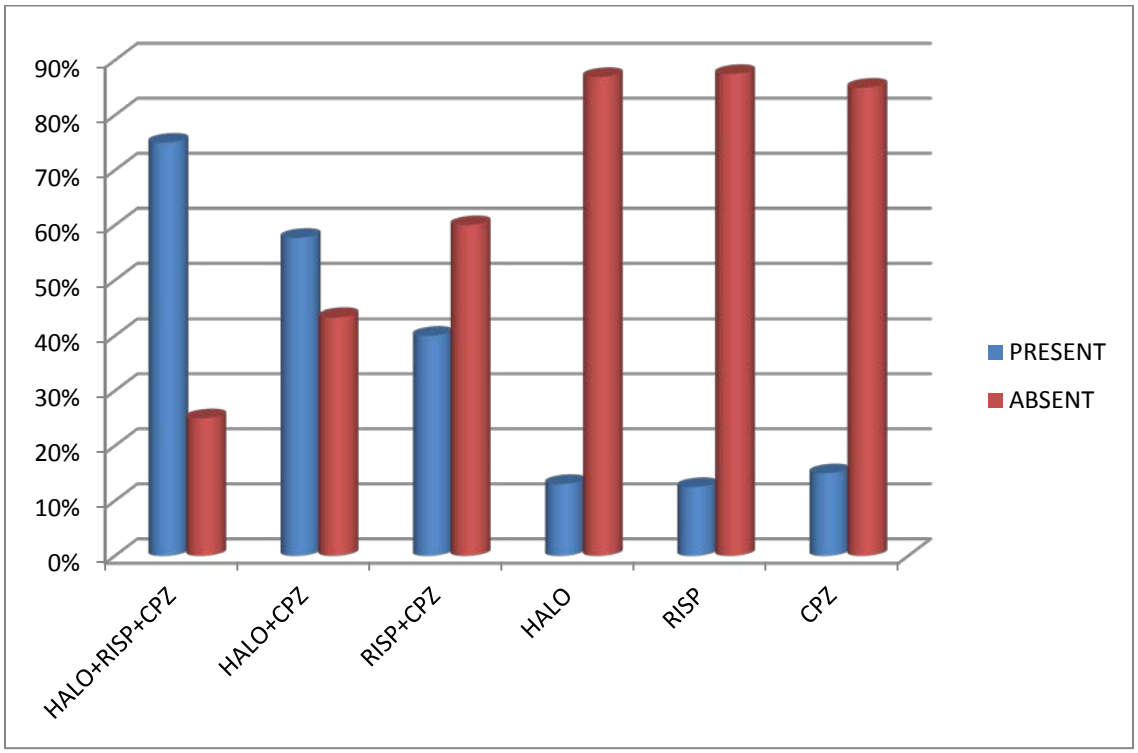
a. 2 cells (33.3%) have expected count less than 5. The minimum expected count is 1.28.

p value = <0.01, proving the association between poly-pharmacy and dry eye disease is significant.


MONO-PHARMACY VS POLY-PHARMACY
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1.5%
23.5%
75.0%
9.4%
62.5%
28.1%
ABSENT
PRESENT
MONO DRUG
DUAL DRUG
MULTI DRUG

DRUG REGIMEN	DRY EYE DISEASE		TOTAL NO OF EYES
	PRESENT	ABSENT	
Halo+Risp+Cpz	6 (75%)	2 (25%)	8
Halo+Cpz	30 (57.69%)	22(43.31%)	52
Risp+Cpz	4 (40%)	16 (60%)	20
Halo	6 (13.05%)	40(86.95%)	46
Risp	4(12.5%)	28(87.5%)	32
Cpz	3(15%)	17(85%)	20
Total	59	141	200

DRUG COMBINATION AND DRY EYE DISEASE



Patients with dry eye disease were given treatment according to the DEWS guidelines.

SUMMARY

1) 32 patients out of 100 patients on anti-psychotic medications for more than 2 years had dry eye disease. Of the 200 eyes evaluated, 59 eyes were found to have dry eye disease.

2) 61.01% of the eyes with dry eye disease were between 41-60 years of age and on treatment.

3) 45.7% of patients had Grade 2 dry eye disease according to DEWS guidelines.

4) Nearly 53.13% patients with dry eye disease were symptomatic. Most common symptom being Foreign body sensation present in 32% cases.

5) Tear film meniscus height was reduced in 93.2% of cases.

6) The Schirmer's test 1, fluorescein staining, tear film break up time were highly diagnostic of dry eye disease.

7) No dry eye associated complications were present in any patients

8) Of the Anti-Psychotic medications used in our study, Dry eye disease was found to be more common with Chlorpromazine(15%) > Haloperidol (13%)> Risperidone(13.5%).

9) Typical antipsychotics (13.95%) showed more prevalence of dry eye disease than Atypical antipsychotics(12.5%).

10) Patients on Multidrug regimen showed more prevalence of dry eye that is nearly 75% than dual (58%) or mono drug regimen(40%). Combination of triple drugs, Haloperidol, Chlorpromazine and Risperidone had more cases of dry eye followed by patients on Haloperidol and Chlorpromazine combination followed by Risperidone and Chlorpromazine combination.

11) The patients who had taken anti-psychotic medications for more than 8 years showed more preponderance for dry eye disease. Nearly 78% of patients had dry eye disease.

CONCLUSION

32 out of 100 patients on anti-psychotic medications for more than 2 years had dry eye disease. Of the 200 eyes evaluated, 59 eyes were found to have dry eye disease. It was found to be more common in people between 41-60 years of age.

Nearly 40% patients were in Grade 3 category of dry eye disease, which if not treated on time can lead to further progression and complication of disease.

The patients who had taken anti-psychotic medications for more than 8 years, especially those who were on multi-drug regimen showed significant preponderance for dry eye disease.

Inspite of the patient's complaints of ocular discomfort , it is difficult to rely on it considering their general state of mind. Our study however emphasizes on the need to give importance to patient's symptoms, so that it can be detected earlier before it progresses .

ANNEXURES

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PROFOMA

Serial no:

Name :

Age:

Sex:

Occupation:

Address :

Ocular complaints:

Associated Systemic illness :

Family history :

Psychiatric disorder:

Treatment:

Duration of treatment:

OCULAR EXAMINATION

	RE	**LE**
Vision		
Eyelids and lashes		

Extra ocular movements

Slit lamp examination

Conjunctiva

Cornea

Anterior chamber

Iris

Pupil

Lens

IOP

TEAR FILM ANALYSIS:

Tear film height:

TBUT:

Schirmers 1:

Schirmers 2:

Fluorescein staining:

IMPRESSION:

ADVICE:

சுயஒப்புதல் படிவம்

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்லி மருத்துவமனை,

பங்கு பெறுபவரின் பெயர் : சென்னை - 600 001.

பங்கு பெறுபவரின் எண் :

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும் :

மனநோயாளிகளுக்கு மனநோய் மருந்தினால் ஏற்படும் கண்ணீர் திரையில் பிறழ்தல் பற்றிய-ஓர் ஆய்வு

பற்றிய ஆய்வு விவரங்கள் எனக்கு விளக்கப்பட்டது, என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த
விளக்கங்களை பெறவும் வாக்கிக்கப்பட்டது.

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்ப்படாமல்நான் இவ் வாய்வில் இருந்து விலக்கிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த பரிசோதனை சம்பந்தமாகவோ. இதை சார்ந்து மேலும் ஆய்வு மேற்கெள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும். மருத்துவர் என்னுடைய மருத்துவ, இதை சார்ந்து மேலும் ஆய்வு மேற்கெள்ளும் போதும் இந்த ஆய்வில் அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக்கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும். பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன்.

மனநோயாளிகளுக்கு மனநோய் மருந்தினால் ஏற்படும் கண்ணீர் திரையில் பிறழ்தல் பற்றிய - ஓர் ஆய்வு

பற்றிய ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதி அளிக்கிறேன். என் உடல் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதைமருத்துவ அணிக்கு தெரிவிப்பேன் என் உறுதி அளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம்

ஆய்வாளரின் கையொப்பம்

நோயாளி தகவல் தாள்

மனநோயாளிகளுக்கு மனநோய் மருந்தினால் ஏற்படும் கண்ணீர் திரையில் பிறழ்தல் பற்றிய - ஓர் ஆய்வு

ஆய்வில் நோக்கம் :

மனநோயாளிகளுக்கு மனநோய் மருந்தினால் ஏற்படும் கண்ணீர் திரையில் பிறழ்தல் பற்றிய-ஓர் ஆய்வு

உண்டாக கூடிய இடர்கள் :

அனைத்து முறைகளிலும் இருப்பது போலவே இந்த முறையிலும் சில எதிர்பாரத இடர்கள் சம்மந்தப்பட்டுள்ளன. சிலருக்கு கண் எரிச்சல் ஏற்படலாம். அதிகமான ஒளி சிலருக்கு கண் கூச்சத்தை ஏற்படுத்தலாம். அதிகமான ஒளி சிலருக்கு கண் கூச்சத்தை எற்படுத்தலாம்.

அந்தரங்கத் தன்மை :

உங்கள் மருத்தவப் பதிவேடுகள் மிகவும் அந்தரங்கமாக வைத்துக் கொள்ளப்படும். மற்ற பிற மருத்துவர்கள் / விஞ்ஞானிகள் இந்த ஆய்வின் தணிக்கையாளர் அல்லது ஆராய்சி ஆதரவாளர்களின் பிரதிநிதிகன் ஆகியோரிடமும் அவை வெளிப்படும். இந்த ஆய்வின் முடிவுகள் அறிவியல் பத்திரிக்கைகளில் பிரசுரிக்கப்படலாம். ஆனால் பெயரை வெளியிடுவது மூலம் நீங்கள் அடையாளம் காட்டப்படமாட்டீர்கள்.

ஆய்வில் பங்கேற்கும் நோயாளியின் கடமைப் பொறுப்புகள் :

உங்களை கவனித்துக் கொள்ளும் மருத்துவருடன் நீங்கள் முழுமையாக ஒத்துழைக்க மேண்டும் மற்றும் உங்கள் மருத்துவரால் குறிப்பிடப்படும் மருந்துகளை தவறாமல் பின்பற்ற வேண்டும் என்றும். என்னென்ன செய்ய வேண்டும். என்னென்ன செய்ய கூடாது என்றும் கூறப்பட்டுள்ளவற்றிலுருந்து சற்றும் விலகக் கூடாது என்றும் நீங்கள் எதிர்பார்க்கப்படுகிறார்கள்.

ஆய்வில் உங்கள் பங்கேற்பு மற்றும் உங்கள் உரிமைகள் :

இந்த ஆய்வில் உங்கள் பங்கேற்பு தன்னிச்சையானது மற்றக் காரணங்கள் எதையும் கூறாமலேயே நீங்கள் இந்த ஆய்விலிருந்து எந்த நேரத்திலும் விலகிக் கொள்ளலாம். எந்த ஒரு நேரத்திலும் உங்களுக்கு திருப்திகரமாக இல்லை என்று உணர்ன்ந்தாலோ அல்லது வேறு ஏதேனும் உடல் நலக்குறைவு உண்டானாலோ. உங்களை கவனிந்து வரும் மருத்துவரிடம் உடனடியாக தெரிவிக்கவும், சிகிச்சை உங்களுக்கு பொருத்தமாக இருக்காது என்று தோன்றினால் உடனடியாக நிறுத்தப்படும். உங்கள் சம்மதம் இன்றியே கூட ஆய்வு நிறுத்தப்படுவது சாத்தியமே.

வேறு ஏதேனும் கேள்விகள். பிரச்சனைகள் பற்றி நீங்கள் கேட்க விரும்பினால் கீழ்க்கண்ட நபரைத் தொடர்பு கொள்ளவும்

மருத்துவர். சௌமியா ஜன்னா

பட்ட மேற்படிப்பு மருத்துவ மாணவி
(முன்றாம் ஆண்டு)
கண்ணியல் துறை,
அரசு ஸ்டான்லி மருத்துவ கல்லூரி,
சென்னை - 01.
போன் : 9962093846

KEY TO MASTER CHART

M	-	Male
F	-	Female
SCH	-	Schizophrenia
PNOS	-	Psychoses not otherwise specified
HALO	-	Haloperidol
CPZ	-	Chlorpromazine
RISP	-	Risperidone
MG	-	Milligrams
OD	-	once a day
BD	-	Twice a day
TDS	-	Thrice a day
A	-	Absent
FBS	-	Foreign body sensation
IRR	-	Irritation
DIS	-	Discomfort
AB	-	Absent

P	-	Present
MIL	-	Mild
MOD	-	Moderate
SEV	-	Severe
MAR	-	Marked
DIF	-	Diffuse
N	-	Normal
RE	-	Right eye
LE	-	Left eye

NAME	AGE	SEX	DIAGNOSIS	TREATMENT	SYMPTOMS	DURATION(YEARS)	TBUT		TEAR FILM HEIGHT		SCHRIMER 1		SCHRIMER 2		CONJUCTIVAL INJECTION		CONJUCTIVAL STAINING		CORNEAL STAINING		SEVERITY OF DRY EYE	
							RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
MALA	28	F	SCH	HALO 1.5MG BD, CPZ 50MG OD	A	2	N	AB	AB	AB	8	2	3	0	A	A	A	MOD	MIL	MAR	2	4
KAMESH	35	M	SCH	HALO 5MG 1/2OD CPZ 100MG 2OD	A	4	N	N	N	N	35	35	28	28	A	A	A	A	A	A	N	N
RADHAKRISHNAN	19	M	SCH	HALO 5 MG BD CPZ 100MG BD	A	4	N	N	N	N	35	35	26	26	A	A	A	A	A	A	N	N
BABU	55	M	SCH	HALO 1.5MG OD	A	5	N	N	N	N	35	35	28	30	A	A	A	A	A	A	N	N
ANANDAN	49	M	SCH	CPZ 100MG 2OD	A	6	N	N	N	N	13	25	9	20	A	A	A	A	A	A	N	N
THRUVAVAKARAN	30	M	SCH	HALO 1.5MG BD	A	8	N	N	N	N	25	15	20	11	A	A	A	A	A	A	N	N
BASKER	42	M	SCH	CPZ 100MG 3 OD, HALO 5MG BD	A	6	N	N	N	N	30	30	25	26	A	A	A	A	A	A	N	N
MOHD. ALI	47	M	PNOS	RISPER 2MG OD,	A	7	N	N	N	N	25	28	22	23	A	A	A	A	A	A	N	N
RAVI	37	M	SCH	HALO1.5MG TDS	A	14	N	N	N	N	30	30	26	26	A	A	A	A	A	A	N	N
PARVATHY	52	F	SCH	RISPER 2MG OD, CPZ 50MG OD	FBS	10	AB	AB	AB	AB	6	0	5	0	A	A	MIL	SEV	A	DIF	2	4
LAKSHMANAN	55	M	DD	HALO 5MG BD CPZ 100MG OD	A	25	N	N	N	N	10	10	6	6	A	A	A	A	A	A	N	2
DHANALAKSHMI	45	F	SCH	CPZ 50 MG OD	A	7	N	N	AB	AB	10	10	5	5	A	A	MIL	MIL	A	MIL	2	2
GEETHA	32	F	SCH	HALO 1.5MG BD	A	7	N	N	N	N	25	25	21	20	A	A	A	A	A	A	N	N
SHANTHI	38	F	SCH	RISP 2MG BD	A	5	N	N	N	N	35	35	30	28	A	A	A	A	A	A	N	N
SRINIVASAN	39	M	SCH	HALO5MG 3OD CPZ 100MG 2 TDS	IRR	9	N	N	N	AB	12	4	18	1	A	A	A	MOD	A	MIL	1	3
GANGADHARAN	43	M	DD	RISP 2MG OD, CPZ 100MG 2OD, HALO 5MG OD	A	11	N	N	AB	AB	6	7	3	3	A	A	MIL	MIL	MIL	MIL	2	2
NALINI	28	F	SCH	HALO 1.5MG BD, CPZ 50MG OD	A	12	AB	AB	AB	AB	8	2	4	0	A	A	A	MOD	MIL	MAR	2	3
IKRAM	46	M	SCH	HALO 5MG 1/2OD CPZ 100MG 2OD	A	3	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
DEVENDRAN	51	M	SCH	HALO 5MG OD CPZ100MG OD	A	11	N	AB	AB	AB	9	5	5	2	A	A	A	MIL	A	MIL	2	3
SEKAR	30	M	PNOS	RISP 2MG OD, CPZ 100MG OD	A	4	N	N	N	N	18	25	14	21	A	A	A	A	A	A	N	N
RAMAN	40	M	SCH	HALO5MG 3OD CPZ 100MG 2 TDS	A	9	N	AB	N	AB	20	6	16	3	A	A	A	MIL	A	A	N	2
IBRAHIM	64	M	DD	RISP 2MG OD	A	8	N	N	N	N	35	35	30	28	A	A	A	A	A	A	N	N
DHANAM	38	F	SCH	CPZ 100MG OD	A	20	N	N	N	N	25	25	20	19	A	A	A	A	A	A	N	N
POURNAMI	50	F	SCH	HALO 5MG OD, CPZ 50MG OD	IRR	10	A	AB	AB	AB	4	4	1	1	A	A	MIL	MIL	MIL	MIL	3	3

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RAMYA	18	F	SCH	RISP 2MG OD	A	3	N	N	N	N	10	10	6	7	A	A	A	A	A	A	2	2
SHANTHI	30	F	SCH	RISP 2MG BD	FBS	11	AB	AB	AB	AB	3	2	0	0	P	P	MIL	MIL	MIL	MIL	3	4
DAMODARAN	58	M	SCH	RISP 2MG OD	A	30	N	N	N	N	30	35	28	30	A	A	A	A	A	A	N	N
GUNASEKARAN	20	M	SCH	HALO 5 MG BD CPZ 100MG BD	A	5	N	N	N	N	30	30	25	25	A	A	A	A	A	A	N	N
SUNDARI	21	F	DD	HALO 5 MG BD CPZ 100MG BD	A	6	N	N	N	N	30	30	25	25	A	A	A	A	A	A	N	N
MUNNIAMMAL	36	F	SCH	CPZ 100MG OD	A	21	N	N	N	N	25	25	18	18	A	A	A	A	A	A	N	N
RAJA	45	M	SCH	RISPER 2MG OD, CPZ 50MG OD	DIS	8	AB	AB	AB	AB	5	1	2	0	A	A	MIL	MOD	MIL	MAR	3	4
YESHUDAS	40	M	SCH	CPZ 100MG OD	A	17	N	N	N	N	22	22	18	19	A	A	A	A	A	A	N	N
MARI	46	M	SCH	RISP 2MG OD, CPZ 100MG 2OD, HALO 5MG OD	A	10	AB	AB	AB	AB	6	6	5	4	A	A	MIL	MIL	MIL	MIL	2	2
VISHWA	35	M	SCH	CPZ 100MG OD	P	23	N	N	N	N	30	25	25	21	A	A	A	A	A	A	N	N
VENKATESH	50	M	SCH	CPZ 100MG 2OD	A	8	N	N	N	N	12	30	6	25	A	A	A	A	A	A	N	N
ANGAMMAL	20	F	SCH	RISP 2MG OD	A	4	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
BASKER	20	M	SCH	CPZ 100MG BD, HALO 5 MG BD	A	4	N	N	N	N	30	30	25	25	A	A	A	A	A	A	N	N
SAMPATH	47	M	DD	RISPER 2MG OD, CPZ 50MG OD	FBS	9	AB	AB	AB	AB	0	3	0	1	P	P	SEV	MOD	DIF	DIF	4	3
KUMARAN	48	M	SCH	CPZ 100MG 2OD	A	7	N	N	N	N	28	13	20	6	A	A	A	A	A	A	N	N
RAJU	21	M	SCH	CPZ 100MG BD, HALO 5 MG BD	A	5	N	N	N	N	30	30	25	25	A	A	A	A	A	A	N	N
FATHIMA	51	F	SCH	HALO 5MG OD, CPZ 50MG OD	IRR	11	AB	AB	AB	AB	3	3	0	0	P	P	MIL	MIL	MIL	MIL	3	3
MUNISHVERAL	35	M	PNOS	CPZ 100MG OD	A	17	N	N	N	N	30	28	26	24	A	A	A	A	A	A	3	3
BABY	45	F	SCH	HALO 5MG BD, CPZ 50MG OD	DIS	21	AB	AB	AB	AB	5	6	3	3	A	A	MIL	MIL	MIL	MIL	3	2
LILY	35	F	DD	CPZ 100MG OD	A	17	N	N	N	N	30	30	25	25	A	A	A	A	A	A	N	N
DURAI	56	M	SCH	RISP 2MG OD	A	28	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
MOHD. SALEEM	20	M	PNOS	HALO 5 MG BD CPZ 100MG BD	A	5	N	N	N	N	35	35	30	29	A	A	A	A	A	A	N	N
THANGAM	42	M	SCH	CPZ 100MG OD	A	19	N	N	N	N	25	25	20	20	A	A	A	A	A	A	N	N
VISHWANATH	60	M	SCH	RISP 2MG OD	A	27	N	N	N	N	35	35	30	29	A	A	A	A	A	A	N	N

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THOMAS	50	M	SCH	CPZ 100MG 2OD	A	8	N	N	N	N	18	25	14	20	A	A	A	A	A	A	N	N
KARTHICK	19	M	PNOS	HALO 1.5MG OD	A	4	N	N	AB	AB	9	8	4	5	A	A	MIL	MIL	A	A	2	2
LATHA	32	F	SCH	RISP 2MG OD, CPZ 100MG OD	A	7	N	N	N	N	23	25	17	18	A	A	A	A	A	A	N	N
DHARMADURAI	56	M	SCH	CPZ 100MG 2OD	A	8	N	N	N	N	25	25	18	19	A	A	A	A	A	A	N	N
ANTONY	52	M	DD	CPZ 100MG 2OD	A	7	N	N	N	N	18	18	13	13	A	A	A	A	A	A	N	N
KALYANI	46	F	PNOS	CPZ 100MG 2OD	A	9	N	N	N	AB	25	10	18	5	A	A	A	A	A	A	N	2
PALLAVI	49	F	PNOS	CPZ 100MG 2OD	A	8	N	N	N	N	26	25	20	18	A	A	A	A	A	A	N	N
RAJKUMAR	68	M	SCH	RISP 2MG OD	A	10	N	N	N	N	35	35	28	29	A	A	A	A	A	A	N	N
SARATH	56	M	PNOS	HALO 5MG BD, CPZ 50MG OD	DIS	34	AB	AB	AB	AB	4	5	3	4	A	A	MIL	MIL	MIL	MIL	3	3
MUNNUSAMMY	55	M	DD	CPZ 100MG 2OD	A	10	N	N	N	N	30	25	25	22	A	A	A	A	A	A	N	N
DHANALAXMI	45	F	SCH	RISPER 2MG OD,	A	9	N	N	N	N	24	24	19	19	A	A	A	A	A	A	N	N
PRAKASH	28	M	SCH	RISP 2MG OD, CPZ 100MG OD	A	6	N	N	N	N	24	18	19	15	A	A	A	A	A	A	N	N
PRASANTH	26	M	SCH	HALO 1.5MG BD, CPZ 50MG OD	IRR	8	AB	AB	AB	AB	5	6	3	3	A	A	MIL	MIL	MIL	MIL	3	2
SUDHA	44	F	SCH	CPZ 50 MG OD	A	7	N	N	N	N	12	12	7	7	A	A	A	A	A	A	N	N
VALLI	43	F	DD	CPZ 50 MG OD	A	7	N	N	AB	AB	10	10	5	5	A	A	MIL	MIL	A	A	2	2
KUPPU	34	F	SCH	HALO 1.5MG BD	A	9	N	N	N	N	25	25	20	20	A	A	A	A	A	A	N	N
SAMY	28	M	SCH	RISP 2MG OD, CPZ 100MG OD	A	5	N	N	N	N	24	20	20	16	A	A	A	A	A	A	N	N
KUPPUSAMY	49	M	SCH	RISPER 2MG OD,	A	8	N	N	N	N	30	24	24	18	A	A	A	A	A	A	N	N
VEDEHI	30	F	SCH	HALO 1.5MG BD	A	8	N	N	N	N	25	25	20	20	A	A	A	A	A	A	N	N
KUMARI	53	F	SCH	HALO 5MG BD, CPZ 50MG OD	BURNING SENSATION	17	AB	AB	AB	AB	2	3	0	2	P	P	MOD	MOD	MAR	MAR	4	3
YELAMURUGAN	45	M	SCH	CPZ 50 MG OD	A	8	N	N	N	N	13	13	8	8	A	A	A	A	A	A	N	N
VELAYUDHAN	32	M	SCH	HALO 1.5MG BD	A	9	N	N	N	N	28	28	22	20	A	A	A	A	A	A	N	N
GURURAJ	30	M	SCH	RISP 2MG OD, CPZ 100MG OD	A	4	N	N	N	N	18	19	14	14	A	A	A	A	A	A	N	N
VEERASAMY	34	M	DD	HALO 1.5MG BD, CPZ 50MG OD	IRR	10	N	N	AB	AB	7	4	5	3	A	A	A	MIL	MIL	MIL	2	3
MANI	30	M	SCH	RISP 2MG OD, CPZ 100MG OD	A	4	N	N	N	N	18	25	4	4	A	A	A	A	A	A	N	N
MURUGAN	43	M	SCH	RISP 2MG OD, CPZ 100MG 2OD, HALO 5MG OD	A	11	N	N	N	N	24	26	20	20	A	A	A	A	A	A	N	N

CHANDRA	52	F	SCH	HALO 1.5MG OD	A	7	N	N	N	N	28	28	22	23	A	A	A	A	A	A	N	N
RADHAKRISHNAN	50	M	SCH	HALO 5MG OD CPZ100MG OD	DIS	12	N	AB	AB	AB	9	4	4	1	A	A	MIL	MIL	MIL	MIL	2	3
DANIEL	31	M	SCH	HALO 1.5MG BD	A	6	N	N	N	N	26	25	22	22	A	A	A	A	A	A	N	N
MESHA	29	F	SCH	RISP 2MG BD	A	6	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
SELUPATHY	32	M	DD	HALO 1.5MG BD	A	10	N	N	N	N	25	17	20	14	A	A	A	A	A	A	N	N
JASMINE	39	F	SCH	RISP 2MG OD, CPZ 100MG 2OD, HALO 5MG OD	A	9	AB	AB	AB	AB	4	5	3	2	A	A	MIL	MIL	MIL	MIL	3	3
VENKATACHALAM	50	M	SCH	HALO 1.5MG OD	A	5	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
ARAVIND	25	M	SCH	HALO 1.5MG BD	A	10	N	N	AB	AB	7	8	4	4	A	A	A	A	A	A	2	2
RAJESH	31	M	SCH	HALO 1.5MG BD	DIS	17	AB	AB	AB	AB	3	7	1	4	A	A	MOD	MIL	MAR	A	3	2
YASMIN	33	F	SCH	HALO 1.5MG BD	A	9	N	N	N	N	30	25	25	21	A	A	A	A	A	A	N	N
MANIKANDAN	49	M	DD	RISPER 2MG OD, CPZ 50MG OD	A	11	AB	AB	AB	AB	4	2	3	0	A	A	MIL	MIL	MIL	MIL	3	3
KRISHNAMURTHY	56	M	SCH	HALO 1.5MG OD	A	6	N	N	N	N	28	30	24	25	A	A	A	A	A	A	N	N
VELARMUTHU	50	M	DD	HALO 1.5MG OD	A	5	N	N	N	N	30	30	24	24	A	A	A	A	A	A	N	N
VELU	24	M	SCH	HALO 1.5MG BD	A	8	N	N	N	N	18	26	15	22	A	A	A	A	A	A	N	N
SOUNDARYA	49	F	DD	RISPER 2MG OD,	A	8	N	N	N	N	30	24	24	18	A	A	A	A	A	A	N	N
KALYANI	55	F	SCH	HALO 1.5MG OD	A	6	N	N	N	N	35	35	29	30	A	A	A	A	A	A	N	N
VAISHNAVI	28	F	PNOS	RISP 2MG BD	A	6	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
LOGANATHAN	42	M	SCH	CPZ 100MG 3 OD, HALO 5MG BD	A	6	N	N	N	N	35	35	29	28	A	A	A	A	A	A	N	N
SAI	33	F	SCH	HALO 1.5MG BD	A	8	N	N	N	N	23	25	18	18	A	A	A	A	A	A	N	N
DURAI	24	M	SCH	HALO 1.5MG BD	A	8	N	N	N	N	18	26	15	22	A	A	A	A	A	A	N	N
GURUSAMY	57	M	DD	RISP 2MG OD	A	29	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N
SRINIVASAN	60	M	SCH	HALO 5MG BD, CPZ 50MG OD	IRR	40	AB	AB	AB	AB	4	6	2	3	P	P	MIL	MIL	MIL	MIL	3	2
KRISHNAAAMAI	34	F	SCH	HALO 1.5MG BD	A	9	N	N	N	N	25	25	20	20	A	A	A	A	A	A	N	N
SYED MOHAMMED	25	M	SCH	HALO 1.5MG BD	A	10	N	N	N	N	35	35	30	30	A	A	A	A	A	A	N	N

RUKAMANI	49	F	SCH	HALO 5MG OD, CPZ 50MG OD	IRR	9	AB	AB	AB	AB	2	2	0	0	P	P	MOD	MOD	DIF	DIF	4	4